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COCHLEAR POTENTIALS IN MAN.*†

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INTRODUCTION.

The electrical response at the round window to sound stimuli has been known for many years. There are two main components: the cochlear potential originally recorded by Wever and Bray in 1930,[10] and the action potential of the VIIIth nerve. The wave form of the latter has two parts termed the N_1 and the N_2 by Derbyshire and Davis in 1935[2] (see Fig. 1). During the past 30 years the cochlear potentials of many different animals, including cats, guinea pigs, mice, rats, dogs, turtles, fishes, snakes, bats, monkeys, marmosets and pigeons, have been studied. The cochlear potential in man was first detected with the aid of headphones by Fromm, Nylen, and Zotterman in 1935.[4] In 1939, a Russian group, Andreev, Arapova, and Gersuni,[1] used the cathode ray oscilloscope to observe the cochlear potential in man. The first picture of the human cochlear potential was published by Perlman and Case in 1941.[7] Lempert, Meltzer, Wever, and Lawrence,[5,6] reported that they were able to obtain responses

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to sound in about one-half of the patients in whom they attempted to record the cochlear potentials.

In 1959, the recording of human cochlear potentials was begun at the Johns Hopkins Hospital, in the hope that they would give information concerning the characteristics of human hearing; also, it seemed reasonable to believe that the data would aid clinicians in evaluating various operative procedures performed on the middle ear, and in the diagnoses of causes of impaired hearing. Four patients were used in the first attempts to record the cochlear potentials. The response from the first patient is illustrated in an earlier article.[8] The second and third patients gave no response, but patient number four had a good response. In 1960, observations on a group of 17 patients were reported[9] with many examples of cochlear potentials in response to pure tones. The VIIIth nerve action potential recorded at the round window was observed in man when a click stimulus was used in this group of patients. The human VIIIth nerve action potential was found to be similar to those observed in the cat.

Measurements of the cochlear potentials and the VIIIth nerve action potentials in man make possible a quantitative physiological assessment of certain phenomena of human hearing. The physiologist can now correlate the perceptive phenomena of the patient, *i.e.*, the audiogram, with the measurable physiological response of the end organ as represented by the cochlear potential and the VIIIth nerve action potential. Patients with normal hearing could not be used to make recordings of cochlear potentials because of the operative risk. The work on a human being, was, therefore, confined to individuals who were either being operated upon for other reasons, or upon those who had no usable auditory function.

Patients with otosclerosis appeared to be a good group to study. The round window niche is routinely exposed at operation. Usually, no granulation tissue is present in the middle ear, and the cochlear potentials may differ before and after the lesions are corrected.

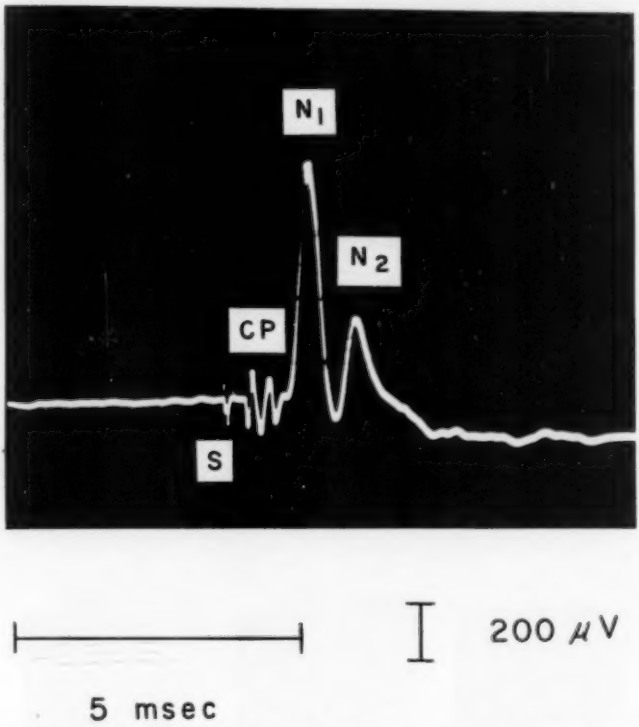

Fig. 1. Electrical change at the round window membrane in response to a click in cat. S, stimulus artifact; CP, cochlear potential; N_1 N_2 neural components of the VIIIth nerve action potentials.

The second group selected for study were children with neurosensory deafness who had no useful hearing. Any information which might be gained as to the etiology of their disease or the location of their defect would be of value in making a definitive diagnosis.

The data for the cochlear potential and VIIIth nerve response for normal hearing have then to be interpolated from these groups. The use of animal experimentation would also be of aid in determining what the normal responses of man should be. Some of the otosclerotics had very little

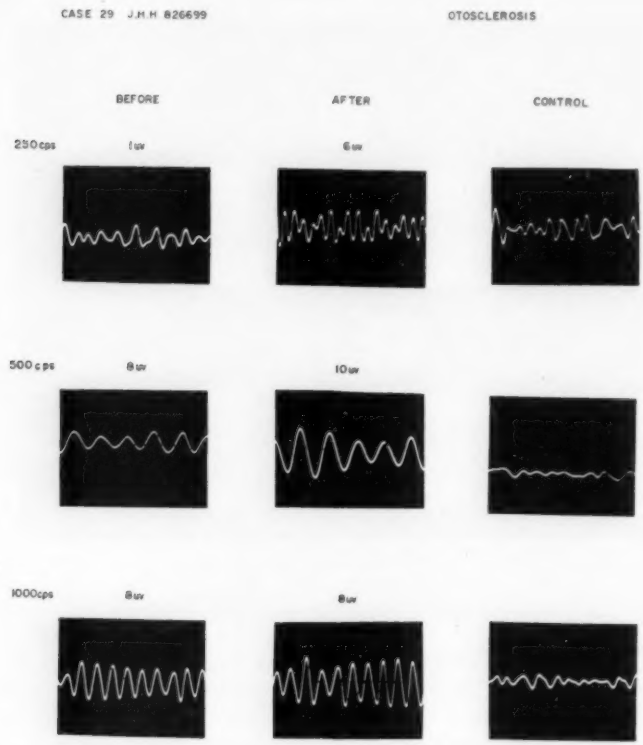

Fig. 2. Case 29, cochlear potentials before and after correction of middle ear lesion. Magnitude of response indicated above each frame. Background noise with tone off is the control.

VIIIth nerve damage and their VIIIth nerve action potentials could approximate the normal VIIIth nerve action potential. The children with neurosensory deafness were all thought to have intact cochlears and from the cochlear potentials of these children inferences could be made about the normal cochlear potential in man.

Attempts have been made to record the cochlear potentials in a total of 34 patients. In 28 of these patients cochlear potentials have been recorded. This report will review the

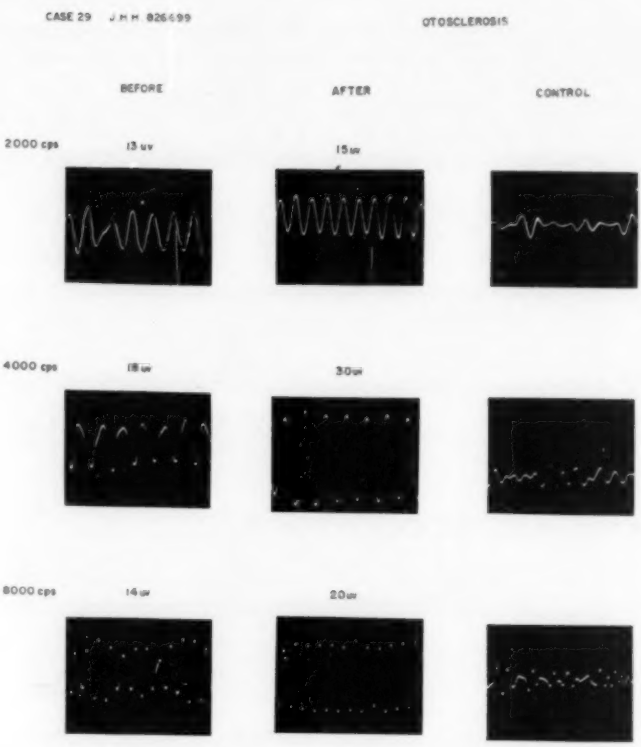

Fig. 3. Case 29, cochlear potentials before and after correction of middle ear lesion. Magnitude of response indicated above each frame. Background noise with tone off is the control.

observations on 12 patients with otosclerosis and seven patients with neurosensory deafness. The remaining 15 patients consisted of 12 patients with tympanomastoiditis; two with trauma and one with syphilis. In these patients the results were too inconsistent and unreliable to be of value.

METHOD.

Recordings are done in the standard operating room, either under local or general anesthesia. The tympanic membrane

is reflected through a transmeatal approach and local anesthetics are not used in the middle ears in any of the cases in the study. A #31 gauge platinum wire with a thin coat of teflon is used as an electrode. One end is flamed in an oxyacetylene torch so that a small ball is formed. The rounded end is placed in the round window niche, and the wire is

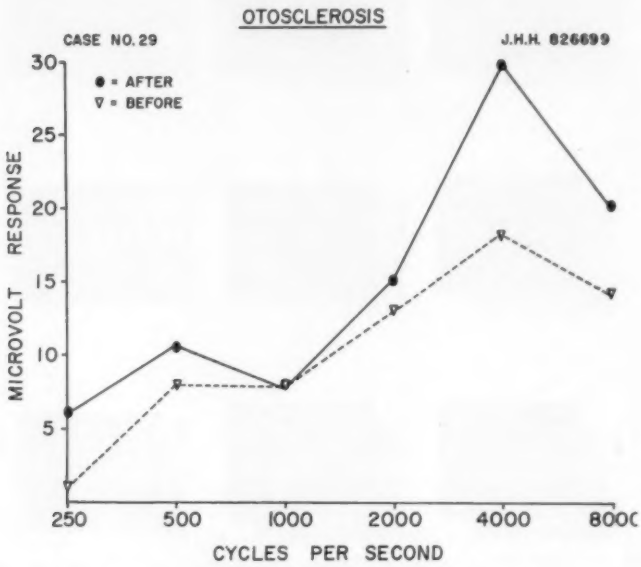

Fig. 4. Case 29, magnitude of cochlear responses plotted before and after lesion corrected.

fixed to the ear speculum with bone wax. If the round window membrane is not seen and a good connection is not made, the round window niche is packed with gelfoam soaked with saline and blood. The electrode is then placed in the gelfoam. The potentials are recorded against an indifferent electrode, a #20 hypodermic needle placed subcutaneously behind the pinna. The patient is grounded from the shield of the cable to the ear speculum.

The electrical response at the round window membrane is

amplified by a Tektronix type #122 preamplifier set to record at 0.8 to 10,000 cps., and is further amplified by a Tektronix type #502 cathode ray oscilloscope. The response is simultaneously viewed on the cathode ray oscilloscope and recorded on the first channel of a four-channel Ampex type 300-4 tape recorder with a frequency range of plus or minus 4 db from 30 to 15,000 cps. The final measurements of the

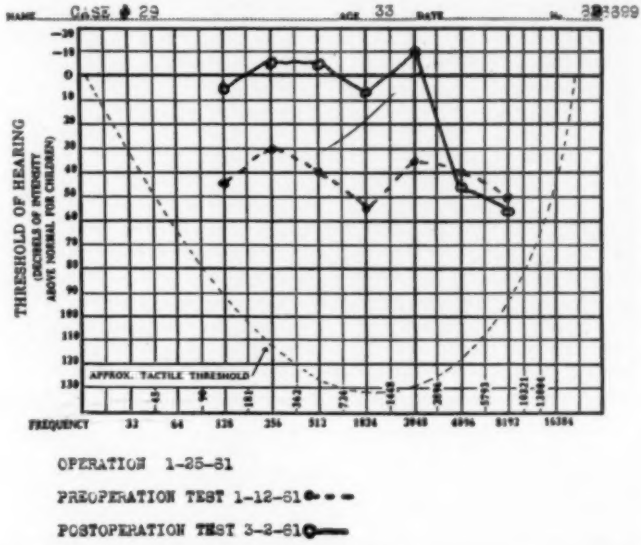

Fig. 5. Case 29, preoperative and 36-day postoperative audiogram.

cochlear potentials are made after the tape is played back through a Kronhite #310AD bandpass filter. The second channel of the tape recorder is connected to a microphone and is used to monitor the operative comment during the recording. The third channel serves as a stimulating channel while the other two channels are recording. The entire tape recorder is activated by a foot pedal which is placed next to the surgeon.

The pure tone stimuli are first recorded on a master tape

and are then transferred to a quarter inch tape which becomes a matrix tape. Multiple tapes for actual patient recordings are made from each matrix tape which provides for uniformity of stimulation for each patient. The stimuli for all cases from 19, are so arranged that all the tones are 90 db above 0.0002 dynes per square cm. as measured at the end

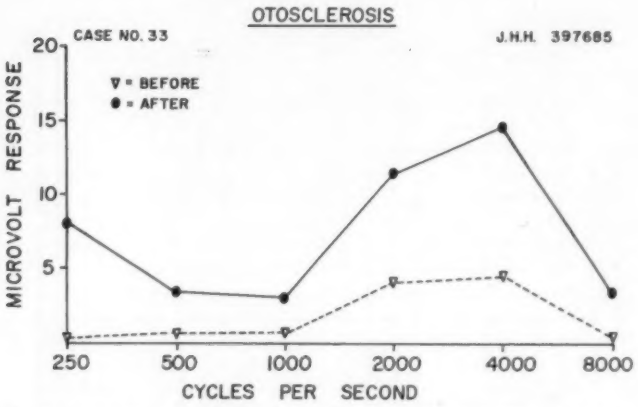

Fig. 6. Case 33, magnitude of cochlear responses plotted before and after lesion corrected.

of a standard ear speculum. The calibrations were done with a Western Electric type 640 AA condensor microphone.

Clicks of 0.075 msec. duration are generated by a Tektronix type 161 pulse generator which simultaneously activates the speaker and is recorded on channel three, the stimulating channel. The pre-recording and transfer of clicks from one tape to another caused too much distortion in the click form. The click recorded on the stimulating channel serves as a marker so that the response to the click could later be found on channel one, the recording channel.

RESULTS.

Part I. Otosclerotics.

Twelve patients with otosclerosis have had recordings of

cochlear potentials and VIIIth nerve action potentials. In 11 of the 12 patients, cochlear potentials were recorded. The only case in which no cochlear potentials were detected was that in which a fenestration of the horizontal semicircular canal was done. In six of the 12 cases, cochlear potentials were recorded both before and after correction of the middle

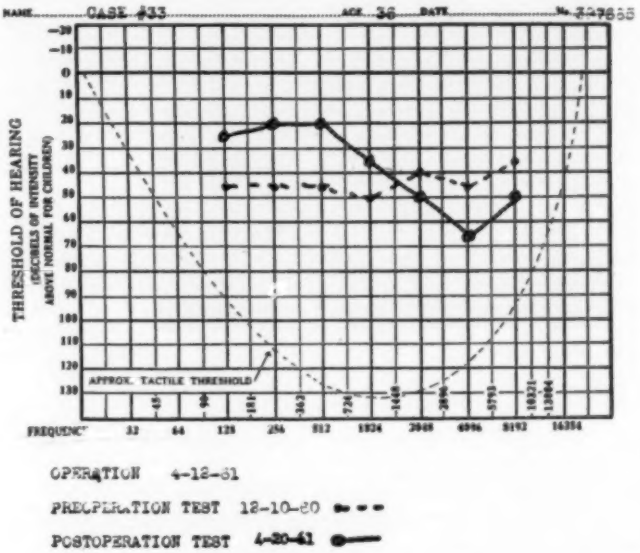

Fig. 7. Case 33, preoperative and eight-day postoperative audiogram.

ear lesion. Five of the six showed an increase in the magnitude of the cochlear potentials after correction. In the sixth case, 34, a loss of perilymph occurred, and a portion of the otosclerotic bone was lost in the vestibule. In this case, after the loss of the perilymph, there was a slight increase in the magnitude of the cochlear potentials for low tones, but the high tones and VIIIth nerve action potential showed a reduction in the amplitude of response.

In Case 29, a 29-year-old man with otosclerosis, the crura

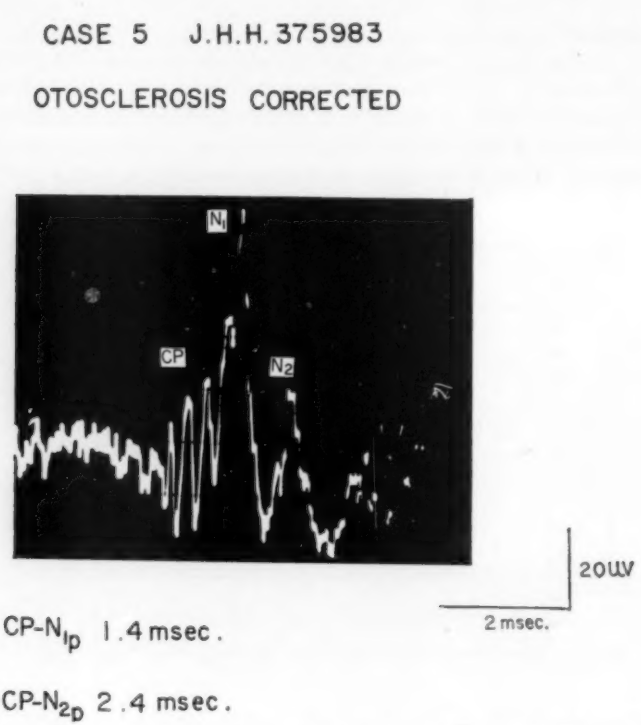

Fig. 8. Case 5, VIIIth nerve action potential. CP-N_1 P and CP-N_2 P latency from beginning of cochlear potential to peak of negative deflection of N_1 and N_2. CP, cochlear potential. N_1 N_2 neural components of VIIIth nerve action potential.

and stapes were removed and a polyethylene strut was placed on the footplate which was then mobilized. The actual changes in the cochlear potentials are illustrated in Figures 2 and 3, and are plotted in Figure 4. An increase in the magnitude of the cochlear potentials at 250, 4000, and 8000 cps. was observed. The preoperative and 36-day postoperative audiograms are illustrated in Figure 5.

Case 33, a 36-year-old woman, shows a picture similar to Case 29. The stapes was firmly fixed in the oval window, and the crura and the footplate had to be totally removed.

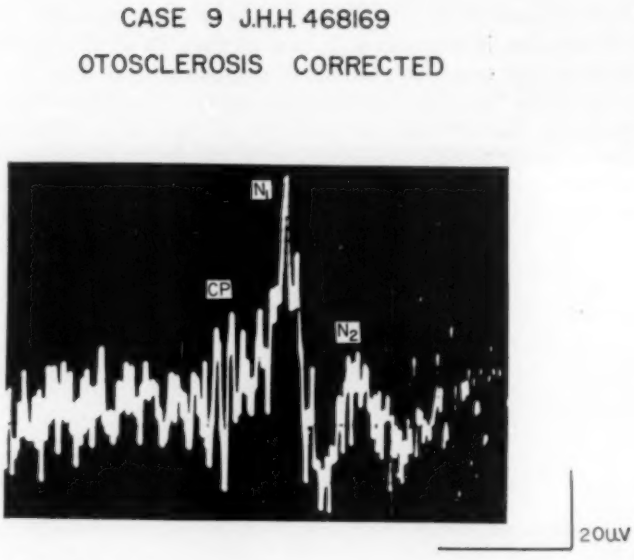

Fig. 9. Case 9. VIIIth nerve action potential. CP-N_1 P and CP-N_2 P latency from beginning of cochlear potential to peak of negative deflection of N_1 and N_2. CP, cochlear potential. N_1 N_2 neural components of VIIIth nerve action potential.

A polyethylene strut was placed on a small piece of gelfoam covering the oval window. The cochlear potentials are plotted in Figure 6. An increase in response to all tones was found. The preoperative and eight-day postoperative audiogram are illustrated in Figure 7. The audiogram for patient 33 shows a reduction in high tones. Such a high tone loss immediately after operation is a common finding in stapes surgery and usually disappears several weeks later.

In seven of the 12 patients with otosclerosis, the response to click was recorded from the round window and found to be similar to those observed in the cat. Five out of seven

patients showed both an N_1 and N_2 response, examples of which are seen in Figures 8, 9, and 10 (see Table I). In the remaining two cases only an N_1 was present (see Fig. 11). The N_1 of all the cases was approximately 50 microvolts in magnitude. The change in polarity of the click stimulus caused a reversal in the cochlear portion of the response to click, but no change was noted in the N_1 and N_2. The action potential was not seen before the correction of the middle ear

TABLE I.

Latency* in Milliseconds of the Action Potential of the VIIIth Nerve Recorded at the Round Window.

	CP to N_1 P	CP to N_2 P	N_2 P minus N_1 P
Cat**	1.0	1.8	0.8
Case 5	1.4	2.4	1.0
Case 9	1.5	2.7	1.2
Case 10	1.2	2.3	1.0
Case 15	2.0	No N_2 Observed	
Case 29	1.6	3.0	1.4
Case 33	1.6	No N_2 Observed	
Case 34	1.4	2.6	1.2
Case 19	1.2	2.0	1.8

*Measurement from beginning of the cochlear potential to the peak of the negative deflection.

**Cat at threshold stimulus.

Note: Cases 5, 9, 10, 15, 29, 33, and 34 Otosclerosis.
Case 19 Congenital neurosensory deafness.
CP—Cochlear potential.
N_1 P—Peak of first negative deflection.
N_2 P—Peak of second negative deflection.

lesion in five of the six cases in which before and after recordings were made. In two of the five the N_1 was present after the middle ear lesion was corrected.

Part II. Neurosensory Deafness.

This group consisted of seven children, all of whom were thought to have a hearing loss secondary to a central nervous system defect. The children, with one exception, could not understand or use in any meaningful way any auditory stimuli. All of these children could be conditioned by psychogalvanic skin response or had some subjective hearing. It was thought that each of these children had an intact middle

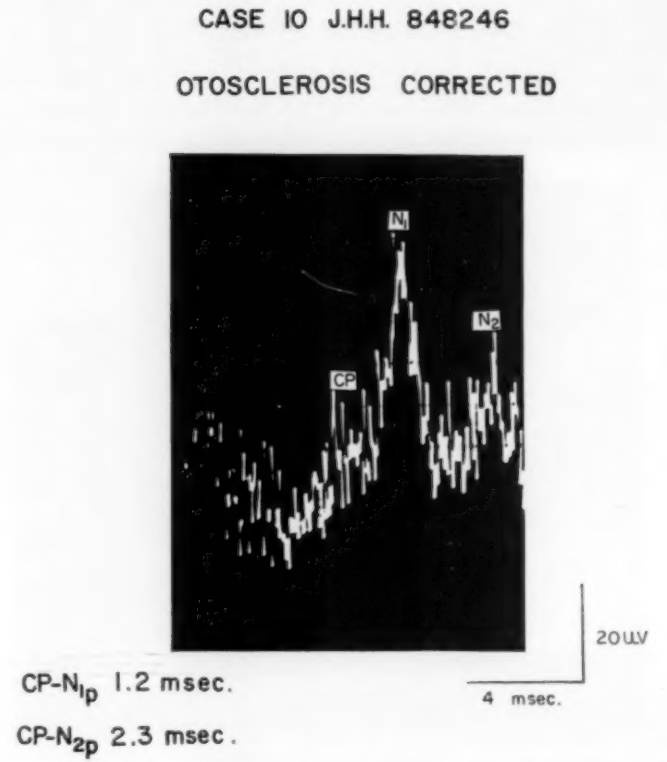

Fig. 10. Case 10, VIIIth nerve action potential. CP-N_1 P and CP-N_2 P latency from beginning of cochlear potential to peak of negative deflection of N_1 and N_2. CP, cochlear potential. N_1 N_2 neural components of VIIIth nerve action potential.

ear and cochlea. One ear of each child was explored. Major or minor middle ear malformations were found in five of the seven children at operation. One case, 28, had no round window, oval window, or stapes. Another patient, 32, was found to have a number of small depressions in the region of the promontory, and the round window niche could not be identified. No cochlear potential was recordable in either of these two cases. The remaining five ears had identifiable round window niches and in all of these cases cochlear poten-

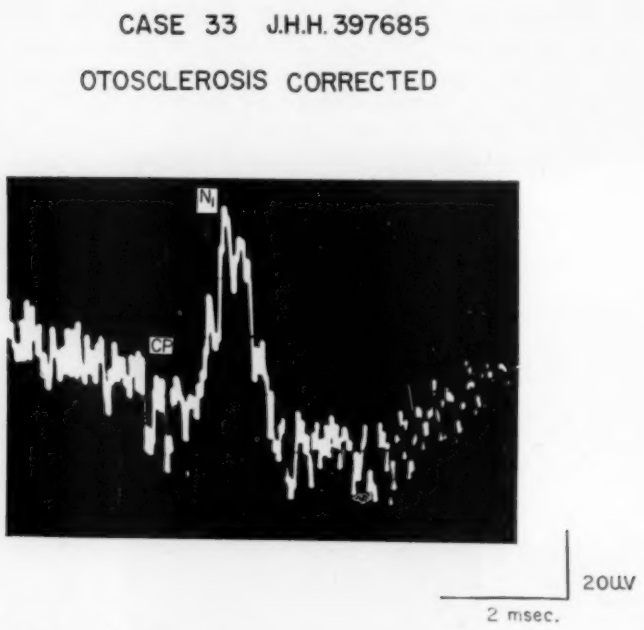

Fig. 11. Case 33. VIIIth nerve action potential showing only N_1 observed. CP-N_1 latency of response from beginning of cochlear potential to peak of the N_1. CP, cochlear potential. N_1 neural component of VIIIth nerve action potential.

tials were recorded. Three of the five ears had thickened membranes in the region of the round window niche, and one of these three had a gelatinous fixation of stapes. In the group of the five in which the cochlear potentials were recorded, one child had a history of kernicterus secondary to RH incompatibility, and another is supposed to have had measles encephalitis. Both of these patients had excellent cochlear potentials with pure tones. Their responses to click appeared to be only the cochlear portion of the response. This observation would seem consistent with lesions present in the central nervous systems of children afflicted with these conditions.

In one of the five cases the typical VIIIth nerve potential was observed. This case, 19, was a two-and-one-half year old child who had no evidence of hearing since the age of four months and was believed to have a hearing loss secondary to brain damage. The child could be conditioned with the psychogalvanic skin response to a 15 to 20 db level. The child had evidence of an intact cochlea and VIIIth nerve as demonstrated by the X-ray, Figure 12. The cochlear potentials of this child are shown in Figures 13 and 14, and are plotted

Fig. 12. Case 19. X-ray of the temporal bone showing internal auditory meatuses, cochlears and labyrinths present bilaterally.

in Figure 15. Note the maximum response was at 4000 cps. The plot is typical for the cochlear potentials of the other children with congenital neurosensory deafness. The VIIIth nerve action potential is shown in Figure 16 and is similar to the other VIIIth nerve action potentials (see Table I).

DISCUSSION.

Recording of the cochlear potential in man has been hampered by two general problems: the first problem is electrical and applies to the techniques of stimulation, amplification,

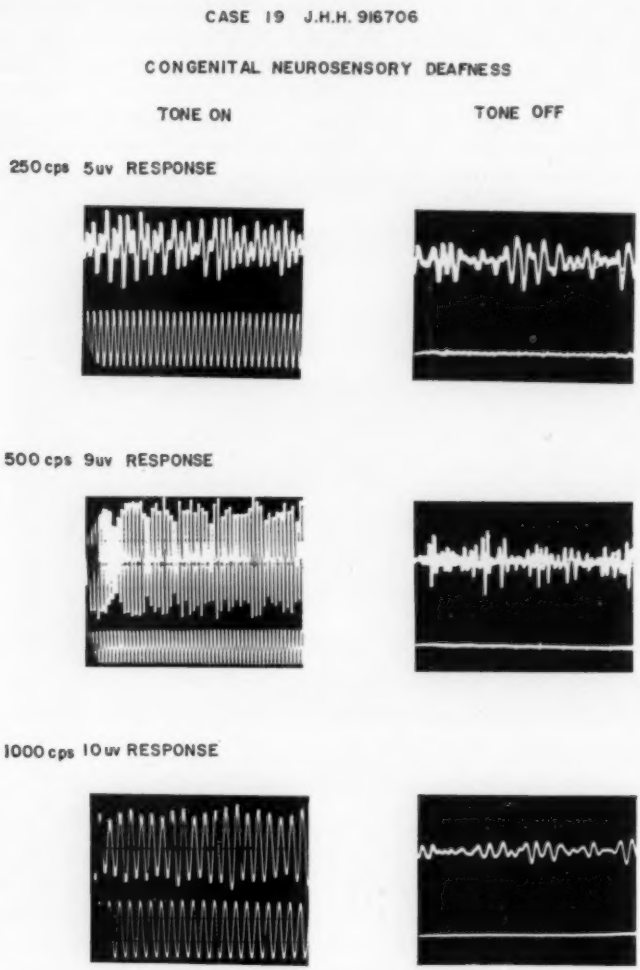

Fig. 13. Case 9, cochlear potentials recorded. Upper trace, response. Lower trace, stimulus.

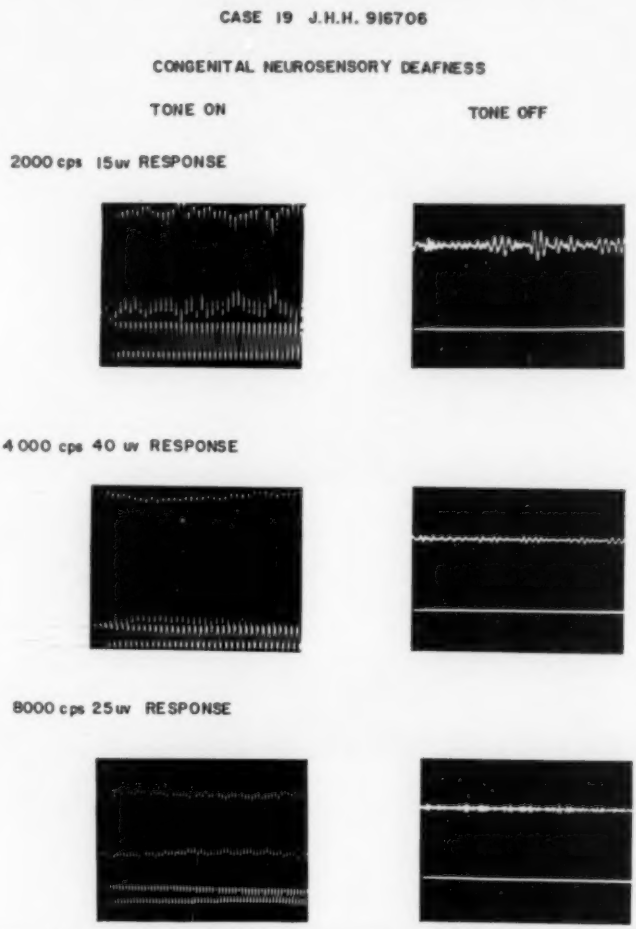

Fig. 14. Case 9, cochlear potentials recorded. Upper trace, response. Lower trace, stimulus.

and recording in a general operating room. It has taken the technical advances of the past 30 years to provide an electrical system which can be used in the ordinary operating room with a minimum of difficulty. This factor is very important in that during the operation there are many considerations with which the experimental physiologist is not faced, such as maintaining rigid asepsis, the patient's well being, and the time that one is allowed to be in the operating

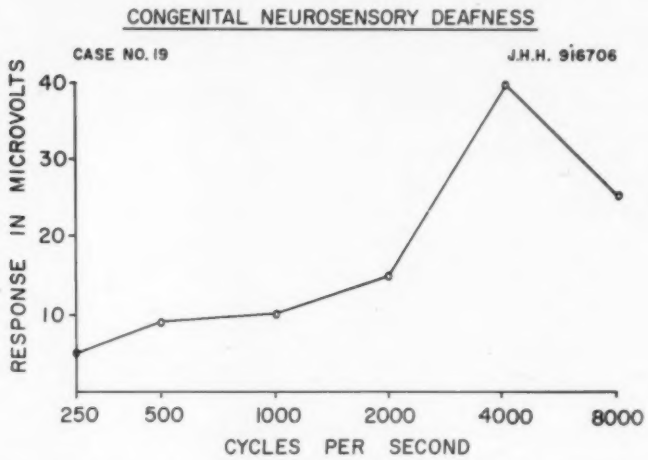

Fig. 15. Magnitude of cochlear potentials plotted. Note the scale of the response is twice as great as in Figures 4 and 6.

room. The use of the multi-channel tape recorder to stimulate and record simultaneously, gives the surgeon complete freedom from the technical electronic difficulties during the operation. All that the surgeon needs to do is to activate the foot switch, and the entire experiment is carried out for him.

The second general problem in the recording of human cochlear potential lies in the anatomy of the human middle ear. The round window membrane often lies deep in the niche. An example of this is illustrated in Figure 17, from the Collection of the Department of Otolaryngology and pre-

pared by Dr. Stacy Guild. The round window membrane was seen in one-third of our cases, and the electrode had to be placed blindly into the niche in the remaining two-thirds. Gelfoam was packed into the round window niche in one-third of the cases and the electrode placed in it. Experiments were carried out in cats to determine whether the gelfoam on the

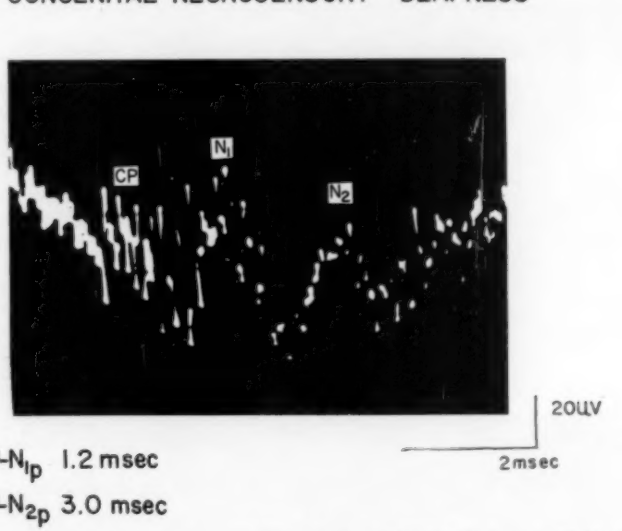

Fig. 16. Case 19, VIIIth nerve action potential. CP-N_1 P and CP-N_2 P latency from beginning of cochlear potential to peak of negative deflection of N_1 and N_2. CP, cochlear potential. N_1 N_2 neural components of VIIIth nerve action potential.

round window niche would affect the magnitude of the cochlear response recorded. Recordings were made by placing an electrode on the round window membrane and then placing a piece of gelfoam on the round window membrane. The electrode was then placed onto the gelfoam. Identical sound stimuli were used, and no difference was found in the magnitude of the cochlear response between the recordings made

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when the electrode was on the round window membrane or when it was on the gelfoam placed on the round window membrane.

Cases of otosclerosis demonstrate that an increase in the magnitude of the cochlear potential is detectable after the conduction mechanism of the middle ear is improved. The

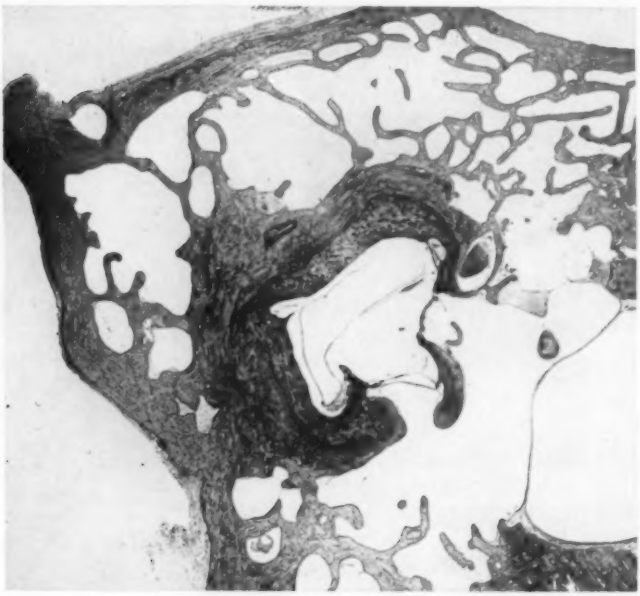

Fig. 17. Section of the middle ear of man. Note that the round window membrane lies deep within the round window niche.

cases which have been illustrated show a definite increase in the magnitude of the cochlear response for both the high and low tones. Relatively, however, the change is much greater for the low tones, for which it may be as much as 600 to 700 per cent. In the high tones the gain is in the order of 50 to 100 per cent. The greatest change in acuity as shown by the audiogram, is found in the low tones; thus, it

would appear that improvement in hearing is related more to the relative change of magnitude of the cochlear potential, rather than to the absolute change.

The variability in the patients with neurosensory deafness was too great to allow for any definite conclusions. Case 19 was felt clinically to have a central lesion, and the recordings obtained may be those of a normal cochlea. If the cochlea is normal, then the cochliogram will represent the function of a normal cochlea. The cochliogram in Case 19 showed a maximum response at 4000 cps. Most of the patients studied, including the otosclerotics, showed a maximal response at 4000 cps. All of the tones which were used were at the same sound pressure level, 90 db above 0.0002 dynes per square cm. The most sensitive portion of the cochliogram, with the tympanic membrane reflected, was 4000 cps.

Man's greatest acuity for hearing is at 1500 to 2000 cps.[3] A discrepancy between behavioral acuity studies and the cochliograms in monkeys, pigeons, guinea pigs, marmosets, and cats has been discussed by Wever.[11] This appears to be consistent with our discrepancy between 4000 cycles for the maximum sensitivity of the cochlea and 1500 to 2000 cps. for the maximum auditory acuity of the organism. This difference may be due in part to a surgical artifact which is introduced by reflection of the tympanic membrane and by the placing of an electrode on the round window membrane.

The recordings of the action potentials of the VIIIth nerve in man allow the clinician and the neurophysiologist to explore the responses of the VIIIth nerve. Eight examples of the VIIIth nerve action potential are tabulated in Table I. They are compared with the action potentials for the cat when a threshold stimulus is used. The measurements are made from the beginning of the cochlear potential to the peak of the negative deflection. The beginning of the cochlear potential was chosen as the initial measurement point because studies done in the laboratory with cats showed that, within limits, the length of the click did not affect the latency of the N_1 and N_2 when the measurement was taken from the beginning of the cochlear potential. The N_1 masks out the

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excessive cochlear portion of the round window response to the long click. If the click is too long, an off-on effect will be noted and a second N_1 can be observed.

The N_1's in the human have a latency ranging from 1.2 to 2.0 msec. from the beginning of the cochlear potential and the N_2's from 2.3 to 3.0 msec. These are all longer than those of the cat at threshold. The difference between the N_1 and N_2 at threshold stimulus in the cat is 0.8 msec. The range for the otosclerotics is 1.0 to 1.4 msec. and appears to be of a similar magnitude to that noted in the cat.

There were two cases in the group of otosclerotics in which the N_2 was not observed. This may be due either to the use of a threshold stimulus or to some damage to the nerve or the nerve connections. In view of the excellent cochlear responses recorded in Cases 15 and 33, the lack of the N_2 has not been explained.

The one case of neurosensory deafness, 19, showed an N_1 with a latency of 1.2 msec. and an N_2 with a latency of 3.0 msec. Both these latencies are within the limits of the other human action potentials observed. The difference between the N_1 and N_2 in Case 19 is 1.8 msec., which is somewhat longer than those in any of the other patients observed; nevertheless, this is probably within the limits of the normal human cochlear response. More cases are needed before a definite statement can be made.

The action potential was seen only in those cases which had a high level of cochlear potential. The N_1 and N_2 were observed in seven out of 12 cases with otosclerosis. There were no cochlear potentials observed at 250 cycles in the five cases in which the action potential was not observed. In only one of the seven cases in which the N_1 and N_2 were observed, was there a lack of cochlear potential at 250 cycles, Case 4. The recording of the action potential of the VIIIth nerve at the round window seems to be related to the amount of cochlear potential generated by the low tones more so than that generated by the high tones.

SUMMARY.

1. The cochlear and the action potentials of the VIIIth nerve can readily be recorded in man.

2. Equipment for the recording of the cochlear and nerve action potential from man in a general operating room has been described.

3. An increase in the cochlear potential with improvement in the conduction mechanism of the middle ear in man has been demonstrated.

4. The latencies of the action potential of the VIIIth nerve in man have been measured.

5. The latencies of the action potential of the VIIIth nerve in man are longer than those in the cat at threshold.

6. The sensitivity of the cochlea under operating conditions differs from the sensitivity for hearing of the organism as a whole.

7. The electrophysiological properties of the human cochlea and VIIIth nerve appear to be similar to those of other species.

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PETROSITIS AND LATERAL SINUS THROMBOSIS DUE TO ANTIBIOTIC-RESISTANT INFECTIONS.*

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INTRODUCTION.

The possibility of an intracranial complication of mastoiditis must constantly be in the mind of the present-day otologist. These infections still occur and he must be as fully aware as his predecessors of the pathways of extension of infection from the temporal bone.

There is an increasing occurrence and seriousness of infections which are relatively resistant to widely available chemotherapeutic and antibiotic agents. The bacterial organisms so frequently found in the chronically discharging ear, especially those of the coliform group, produce infections which respond poorly to treatment with these drugs. Infections deep in the temporal bone may lie dormant under ameliorating antibiotic therapy, only to allow a final rush of bacterial invasion of the brain and meninges at a later date. Petrositis may occur even though it may have been initiated by disease apparently cured months previously. Infections of the brain may not be eradicated with even the most intensive antibiotic therapy and may flare up again after years of quiescence.

Administration of antimicrobial agents may alter the clinical and laboratory findings and disastrously delay exploration and drainage of pus or removal of diseased bone.

In light of personal experience and study of the literature, the diagnostic aspects and treatment of petrositis and lateral sinus thrombosis with their resulting complications of meningitis and brain abscess, are discussed in this paper.

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REVIEW OF LITERATURE.

PETROSITIS.

Baldenweck,[1] in 1908, first completely described apical petrositis; but it was not until more than twenty years later that Eagleton,[2] Kopetzky and Almour,[3] and Ramadier[4] revived interest in this condition. In 1932, Lillie and Williams[5] reported early experience with petrous pyramid infections which were encountered at the Mayo Clinic. Guild,[6] in 1935, described the normal and pathological anatomy of the petrous pyramid in regard to suppuration of this region.

Various surgical methods for drainage of the petrous apex were described. Among the best-known methods were Eagleton's unlocking of the petrous pyramid,[7] Kopetzky's and Almour's,[3] and Ramadier's[4] drainage of the petrous apex, and Frenckner's[8] approach through the geometric base of the pyramid. Lempert,[9] in 1936, approached the petrous apex along the internal carotid artery as had Ramadier, but advocated complete apicectomy rather than apicotomy.

Even after the advent of the sulfonamide compounds and penicillin, Thornell and Williams[10] emphasized the need of adequate primary surgical treatment in instances in which symptoms of petrous involvement developed; they discouraged dependence on chemotherapy alone.

Niho, *et al.*,[11] pointed out that the symptomatology of petrositis has often been erroneously confused with Gradenigo's syndrome; *i.e.*, trigeminal neuralgia and abducens paralysis associated with a discharging ear. Gradenigo's syndrome may occur as a complication of apical petrositis with inflammation of the dura over the apex of the pyramid or with the development of an extradural abscess in this region. On the other hand, infection may be present in the petrous apex, and no such symptoms of this syndrome will occur if this inflammation remains within the confines of the temporal bone.

Apical petrositis has been infrequently reported in recent otolaryngological literature. DeWeese,[12] in 1958, presented three cases of disease involving the petrous portion of the

temporal bone and emphasized the principal symptoms, "Lest we forget that this condition still occurs." The same year Morrow reported a case of suppurative petrositis with Gradenigo's syndrome.

SURGICAL ANATOMY.

Lempert[13] suggested that for the purpose of surgical orientation the temporal bone be divided into two portions. This he felt necessary, if surgical intervention on the diseased pyramid was contemplated. He divided the pyramid into, first, the basal-labyrinthine portion; second, the apical carotid portion. The basal labyrinthine portion was composed of:

a. The labyrinthine bony structure.

b. The structure made up of the perilabyrinthine cell groups.

The apical-carotid portion consisted of:

a. The petrosal course of the internal carotid artery.

b. The cellular bone structure lying partly superior and mostly posterior to the transverse course of the carotid canal.

The perilabyrinthine cells are accessory cell groups which develop in connection with mastoid process. The cells of the petrous apex are independent outgrowths from the tympanic cavity near the orifice of the Eustachian tube. These petrous tip cells always lie posterior and superior to the carotid artery and have a simple pattern related to the carotid canal.

Anson, Wilson, and Gaardsmoe[14] studied the cell groups of the petrous pyramid by wax plate reconstruction and found four groups of cells tending to encircle the carotid canal. One group extends along the carotid canal posterolaterally as far as the apical turn of the cochlea; another extends upward above the carotid canal and then downward on its posteromedial aspect; a third group extends forward, lying anteromedially along the course of the auditory canal and beneath the turn of the carotid canal to extend into the walls of the

jugular and mandibular fossae; and the fourth posterior group extends almost to the basal turn of the cochlea and internal auditory meatus, but not above or below the labyrinth. There is no continuity between the mastoid and petrous cell groups, although they may lie adjacent to each other.

These anatomical cell tracts act as direct pathways of extension of infection from the middle ear cavity; and, according to Lindsay,[15] osteomyelitis of the petrous pyramid is usually due to extension by this route. This, however, does not rule out the possibility of extension of infection to the petrous apex by way of the perilabyrinthine cell tracts which lie contiguous to the apical cells.

PATHOLOGY.

According to Niho, *et al.*,[11] there is no difference anatomically, embryologically, or histologically between the mastoid cells and the petrous cells or between the bone tissue of the mastoid portion of the temporal bone and that of the petrous pyramid; likewise, they state that there is no difference between the two tissues histopathologically in suppurative inflammation. The petrous pyramid, the mastoid portion, and the tympanic cavity (namely, the deep and superficial parts of the temporal bone) are inseparably connected. Histopathologically, mastoiditis with petrositis constitutes osteomyelitis of the temporal bone.

In observing the bone pathology there is at first an acute suppurative inflammation (ultimately leading to the formation of an abscess), which gradually extends to the surrounding tissues. The epithelial lining disappears, and severe inflammation of the bone canaliculi appears at the same time. Finally, the bone lamella become indistinct, bone nuclei become darker and smaller, and bone tissue degenerates and becomes carious.

The inflammation then changes from the acute stage to the subacute or chronic stage. Granulation tissue increases, together with new blood vessels, gradually organizing the abscess. Finally, the abscess is replaced by inflammatory

granulation. The granulation tissue surrounds the bone tissue, and the cells develop to bone cells. As soon as the inflammation disappears, the epithelium of the cells of the temporal bone regenerates and increases, but these epithelial cells which are naturally flat and single layered become tall and cuboid. The granulation tissue in the favorably-progressing part becomes scar tissue.

The histopathologic changes may be severe or slight in any single temporal bone. If the inflammation is of maximal intensity, the lining tissue, bone, and marrow are affected at the same time and rapidly become necrotic. Pneumatic cells, bone tissue, and surrounding tissue as well are affected by inflammation which often extends to the dura. Once the bone canaliculi in the marrow tissue are invaded, be it by hematogenous spread or by direct extension, the reaction to the bacterial invasion is the same.

LATERAL SINUS THROMBOSIS.

The literature of the past decade relating to lateral sinus thrombosis calls one's attention to two things: first, that the signs and symptoms often do not coincide with the classical picture; second, that the infecting organisms are often insensitive to antibiotic therapy.

It is evident that lateral sinus thrombosis still does occur, although Courville,[16] after reviewing 9,737 consecutive autopsies at the Los Angeles County Hospital from 1949 to 1954, did not find a single instance of lateral sinus thrombosis as a cause of death.

Chao[17] reported venous sinus thrombosis occurring as a complication of acute and chronic otitis media in 1 per cent of 1,244 patients studied. This occurred most often as an acute exacerbation of chronic disease.

Reading and Schurr[18] at Guy's Hospital in London concluded that thrombosis of the sigmoid sinus has become quite rare in acute mastoiditis, but remains at about the same per cent of occurrence in chronic mastoiditis. They state that with antibiotics the patient may not have the picture of chills and

fever that made the complication more easily recognized in the past, but that when the condition is suspected the lateral sinus should be uncovered during the mastoid operation.

Cirillo[19] warns of the danger of antibiotics masking the signs and symptoms of intracranial spread of infection. He stresses the importance of making a specific pathologic diagnosis and of adequately using proper antibiotics, as well as of exposing suppurative foci according to well-established principles of otologic surgery.

Harpman[20] points out that in patients with lateral sinus thrombosis who are taking antibiotics, the rigors, pyrexia, metastatic septopyemic manifestations, and tenderness of the lymph glands along the internal jugular vein may not be present. The white cell count or red blood cell sedimentation rate may not be elevated. Jugular compression tests, therefore, become most important in making the diagnosis. He emphasizes the importance of early determination of the antibiotic or chemotherapeutic sensitivity of the infecting agent, because the first line of treatment is systemic administration of the appropriate antibiotic.

Krajina[21] points out that the mixed bacterial flora found in chronic ear infections produce a milder clinical picture, but one which is likely to produce a well-developed thrombosis without the patient having experienced severe symptoms; however, the later stage of thrombosis may be severe if the infection is not controlled by surgery.

Reports in recent years (Krajina,[21] Morrow,[22] McGovern and Khuri,[23] Snitman, *et al.*,[24] Silcox,[25] and Bradburn[26]), indicate that the presence of lateral sinus thrombosis is often caused by bacterial organisms resistant to the antibiotics administered. These resistant bacterial infections have often been due to Gram-negative bacilli. These organisms are most commonly found in chronically discharging ears.

TREATMENT.

The facts of anatomy, physiology, and pathology of the venous channels surrounding the temporal bone must underlie

treatment of otogenic blood stream sepsis. No attempt at a detailed review of these shall be made. Mention, however, is made of the fact that cerebral and cerebellar veins without valves join the lateral sinus and that infection is spread by retrograde thrombosis.

There is no complete agreement on the surgical treatment of lateral sinus thrombosis, but the consensus is that pus must be drained and suppurating thrombi must be removed from the sinus (Harpman,[27] Tamari and Henner,[28] Cirillo,[19] Watkyn-Thomas[29]). Kimmick and Myers[30] feel that the jugular vein should be ligated early in the course of surgery if a thrombus is discovered at operation. This is done in fear of dislodging an embolus into the general circulation. Cawthorne[31] believes ligation of the jugular vein is more useful in the preantibiotic era in order to prevent rapid and massive invasion of the blood circulation by the bacteria or toxins. Today, if the thrombus is eliminated by surgery, there is less need for ligation, since antibiotics may destroy bacteria and eliminate toxins. In his opinion, however, ligation is indicated when purulent thrombophlebitis descends toward the jugular vein or sepsis persists in spite of antibiotic therapy and adequate local therapy of the sinus. These views are shared by Harpman[27].

CASE REPORTS AND COMMENTS.

CASES OF PETROSITIS.

This group consists of three cases of suppurative petrositis, all of which had had symptoms or signs of dural involvement over the apex at some time during the course of the infection. Although antibiotics had been given in each case, surgical removal of the apical focus of infection was necessary before the patients recovered.

In Case 1, there was not only a facial paralysis and labyrinthine fistula secondary to mastoiditis, but also a Gradenigo's syndrome secondary to apical petrositis. It seems probable that infection progressed to the petrous apex along the necrotic pericarotid cell tract found during the mastoidectomy.

Cases 2 and 3 emphasize the fact that the presence of active bone disease in the petrous apex may remain silent for months at a time after antibiotic therapy only to manifest itself at a later date. In Case 2, meningitis recurred four times as a result of a remaining apical focus of infection. The presence of remaining disease in the petrous apex in Case 3 was suspected only after persistent deep pain in the ear and behind the eye which, in all likelihood, was produced by dural irritation over the apex.

Case 1. A. R., a 24-year-old white male, was admitted February 8, 1952, because of a left-sided facial paralysis of three days' duration. Ear drainage had been intermittent since early childhood, but a profuse sanguineous discharge from the left ear began one month prior to admission. This was followed by headache, vertigo, nausea, vomiting, ear pain, chills, fever, and numbness over the left side of the face. Penicillin had been given by his family physician.

Examination on admission revealed a temperature of 100.6° F., pulse 64, and respirations 16. There was a profuse odorous, yellow-brown discharge in the left ear canal and granulation tissue in the middle ear. There was a severe conduction loss of hearing, but bone conduction remained normal. Spontaneous horizontal nystagmus to the right was present, lateral motion of the left eye was impaired, and the left corneal reflex was hypoactive. Sensation over the left side of the face was disturbed, and complete and total left-sided peripheral facial paralysis was present.

Laboratory findings included a leucocyte count of 15,500 with 74 per cent neutrophils. X-ray of the left ear and mastoid revealed diffuse cloudiness of the left mastoid process with cellular destruction and involvement of the petrous tip.

Course in the hospital: The patient was started on penicillin, dihydrostreptomycin, and gantrisin. On February 10, a radical mastoidectomy was done with exenteration of the petrous apex. The mastoid and middle ear were filled with granulation tissue. There was a fistula into the horizontal semicircular canal. The Fallopian canal had been eroded, and the facial nerve was covered with granulation tissue; this was removed and the nerve was decompressed throughout its mastoid course. The postauricular incision was extended, and the zygomatic root and bone over the posterior portion of the temporomandibular joint were removed. The carotid artery was uncovered, and soft bone and granulation tissue removed to the petrous apex where the cell structure was involved with osteomyelitis. This diseased bone was thoroughly removed and the apex drained with a small rubber catheter drain.

The patient's temperature remained normal after surgery. Three days later he was free of vertigo, normal sensation had returned to his face, and he had unrestricted eye movements. Facial function markedly improved within a week, and recovery from the facial palsy was complete within two weeks. Antibiotic therapy was maintained for three weeks after hospital dismissal and the patient remained well.

Case 2. R. U., a 44-year-old diabetic and alcoholic white male, was admitted on March 4, 1958, in a state of coma. There had been two previous admissions, in August, 1956 and July, 1957, for head injuries following acute alcoholism. Another admission six months before had been

for pneumococcic meningitis which followed an infection of his right ear. Severe or total hearing loss in the right ear had followed the head injury in 1957. Two days prior to admission on March 4, he developed pain in the right ear and became lethargic.

Examination showed the patient to be comatose. His temperature was 101.6° F. There was nuchal rigidity and positive Brudzinski's and Kernig's signs. The Babinski reflex was positive on the right. His right tympanic membrane was injected, the landmarks were absent, and a scanty purulent discharge was present in the ear canal. The spinal fluid was grossly purulent. Laboratory findings showed pneumococci in the culture of the spinal fluid and ear drainage. Mastoid X-rays showed increased density throughout the entire bone.

Course in hospital: Penicillin, 15,000,000 units, was given intravenously q. 6 h. and chloramphenicol 0.5 gm. I.M. q. 6 h. When the clinical response was unsatisfactory after three days of this therapy, and the patient was still in a comatose state, a modified radical mastoidectomy was performed. Soft bone and granulations were removed. The sigmoid sinus and dura of the middle and posterior fossae were explored but showed no evidence of localized inflammation. The patient was alert and rational the following day and continued to improve rapidly.

He was discharged ten days after the mastoidectomy and was instructed to continue penicillin therapy at home.

Subsequent hospital admissions: The patient was treated for acute otitis media in July of 1959 and responded to penicillin given intravenously 20,000,000 units twice daily.

In September, 1959, he was again hospitalized for pneumococcic meningitis which followed pain, swelling, and drainage of the right ear. Recovery was made after large doses of penicillin and chloramphenicol. The ear became dry. Instructions again were given to the patient to maintain penicillin therapy at home. He failed to do this.

On March 3, 1960, severe deep pain developed in the patient's right ear, which radiated to the vertex. This was followed again by frank meningitis, which, for the fourth time, was found to be due to the pneumococcus.

Response to penicillin was satisfactory. Because of the recurring episodes of meningitis, all pneumococcic in type, it was decided to explore the right mastoid further. On April 14, 1960, a mastoid exploration was made through an endaural approach. Perilabyrinthine cell tracts were searched for above, posterior to, and below the labyrinth; and although the three canals were skeletonized, a lead to the petrous apex could not be discovered. A radical mastoidectomy was completed. Granulation tissue was present in both oval and round windows, and since no hearing remained in the ear, a wide opening into the labyrinth was made by removing bone and granulation between the two windows. After removing bone anteriorly to gain better exposure, a tract of necrotic bone was found. The carotid artery was uncovered and the tract followed to the petrous apex, where pus, soft bone, and granulation tissue were present. Thorough removal was made with a small curette, and the apex was drained. The postoperative course was without incident, and the patient has remained well.

Case 3. R. J., a 38-year-old white female, was admitted February 2, 1960, with a complaint of severe pain, which had been present for several months, deep in her right ear. This pain, which was more severe at night, radiated behind the right eye. Both tympanic membranes had been perforated since early childhood. Four years previously, she had had pneumococcic otitic meningitis which was medically treated. At that time, a

right facial and right abducens paralysis had been present, but function had subsequently returned. In September, 1959, a right radical mastoidectomy had been done for chronic mastoiditis.

Examination on admission revealed a fully conscious, alert woman. A small amount of purulent discharge was present in the middle ear. Neurologic examination revealed no abnormalities.

Laboratory examination of the blood and spinal fluid showed normal findings. Skull X-rays were normal. Mastoid roentgenograms showed the defect produced by previous mastoid surgery as well as diffuse clouding of the petrous apex. An electroencephalogram showed diffuse, slow dysrhythmia which was thought to be the result of the residuals of her meningitis.

Course in hospital: On February 27, 1960, the right mastoid was explored through an endaural incision. The sigmoid sinus and the dura of the posterior and middle fossae were exposed and found normal. The semicircular canals were outlined, and purulent perilabyrinthine cell tracts were found below the labyrinth and within the arch of the superior semicircular canal. A necrotic cell tract along the carotid artery was followed to the petrous apex, and pus and granulation tissue were encountered and removed. Postoperatively, the patient was relieved of her pain and was discharged on March 7, 1960, in good condition.

CASE REPORTS OF LATERAL SINUS THROMBOSIS.

This group consists of seven cases in which the lateral sinus was involved by infection in varying stages of development as well as by fully developed septic thrombi. The lateral sinus was the portal of entry to the posterior fossa in two instances, which led to formation of cerebellar abscesses (Case 4 and Case 5). In six of the seven cases, other mastoid complications accompanied the lateral sinus infection. In addition to the two cerebellar abscesses, there were two subperiosteal abscesses (Case 6 and Case 7), an epidural abscess (Case 8), and finally a case with a facial paralysis and a labyrinthine fistula (Case 9).

Case 4. R. K., an 18-year-old white male, was admitted to the neurosurgical service on November 7, 1952, in a state of coma. One month previous he had been treated for meningitis at the contagious disease hospital, where therapy had included penicillin, streptomycin, and Cortisone. Improvement occurred, and he was sent home. The day prior to his admission he had headache and vomiting. Chronic drainage from the right ear had been present since three years of age.

Examination on admission revealed a patient in coma, rousing only to painful stimulation. He had a spiking temperature elevation. The eyes deviated to the left, and there was slight blurring of the right optic disk. The Babinski reflex on the right was positive, but all other reflexes were present and equal. The presence of a draining right ear was noted, and a brain abscess was suspected, but localization was not clear.

Course in the hospital: The patient was taken to the operating room and a trephine opening was made in the right temporal region. A brain

cannula was inserted into the temporal lobe until the ventricle was reached at a normal depth and clear cerebrospinal fluid came forth with great pressure. Subsequently, burr openings were made over the right temporal, and both frontal areas and the lateral ventricles were cannulated, but no abscess was found. A number 8F catheter was placed into the right lateral ventricle through the frontal trephine opening. The patient temporarily improved.

Ten days later, after a preliminary ventriculogram, a right suboccipital craniotomy was done. An abscess was reached with a brain cannula 2 cm. from the surface. Overlying cerebellum was removed, as well as portions of the abscess capsule. Purulent material was evacuated, but the abscess was so large, friable, and adherent that total resection was not attempted. A rubber tube was placed into the abscess cavity and brought out through the incision. Purulent secretions sent for culture revealed an anaerobic, Gram-negative bacillus of the genus Bacteroides.

The patient continued to have gradually rising and spiking temperature elevations and a purulent but sterile spinal fluid. An internist, specialized in antibiotic therapy, initially gave him 10,000,000 units of penicillin intravenously twice daily. He instilled streptokinase and streptodornase into the ventricular tube to relieve a block between the lateral and third ventricles. Subsequently, chloromycetin, streptomycin, aureomycin, neomycin, and sulfadiazine were given intravenously. Streptomycin, neomycin, and polymixin B were instilled into the abscess cavity. The patient remained semicomatose.

An otologic consultation was held December 3, 1952. A foul, purulent discharge was present in the right ear canal; the tympanic membranes had been destroyed, and the middle ear was filled with granulation tissue. The Tobey-Ayer test was positive, and mastoid roentgenograms showed diffuse clouding, absence of cell structure, and periantral sclerosis. It was suspected that the portal of entry to the posterior fossa had been by way of the mastoid and sigmoid sinus.

A mastoid exploration was done the same day through a postauricular approach. Upon removing the mastoid cortex, thick yellow pus welled forth. Soft infected bone extended back over the sigmoid sinus. The vessel was surrounded by pus and granulation tissue and was completely thrombosed. The infected thrombus extended from the horizontal portion of the sinus to the jugular bulb and was removed until free bleeding was obtained at both ends. The vessel was externally packed. The posterior fossa dura below the sinus appeared thickened and inflamed, but no fistulous tract was found in this area. A radical mastoidectomy was completed after removing a cholesteatoma and granulation tissue from the middle ear. Exploration of the middle fossa dura above the mastoid revealed no abnormality.

The patient made a slow recovery and was discharged from the hospital one month later. He had residual mental retardation, impaired hearing bilaterally, instability, and intermittent epileptic seizures. He finally reached a plateau on his physical rehabilitation.

Subsequent hospital admission: Six years later he developed severe headache, vomiting, and increased drowsiness. Examination on admission revealed a drowsy patient who had thick speech, impaired hearing, difficulty in walking, and incoordination of his right arm and leg. The mastoid cavity was healed but contained epithelial debris. The right suboccipital decompression area was bulging and 15 cc. of creamy pus was aspirated. The same Gram-negative bacillus, a Bacteroides species, was cultured.

The right suboccipital area was reopened, and an abscess found behind

the temporal bone and in the superior and lateral aspects of the posterior fossa. An abscess approximately 5 cm. in diameter was dissected and removed *in toto*.

Chloramphenicol and penicillin were given intravenously and neomycin by mouth until September 3, 1958. A pseudomeningocele caused a swelling over the incision line for a short time, but improvement continued. The patient was discharged on September 6, 1958, after having recovered to the state which existed prior to the second abscess formation.

COMMENTS.

This case is very instructive for several reasons: first, it illustrates the very serious dangers which may result from neglect of a mastoid cholesteatoma. Second, it emphasizes that first in importance in treatment of a brain abscess producing increased intracranial pressure, is relief of that pressure by decompression. Finally, it points out the extreme resistance of the anaerobic bacillus which produced the cerebellar abscess. The massive, long-continued use of antibiotics of a wide variety, given by every possible route, failed to eradicate the infection in the cerebellum, with a second abscess resulting six years later.

Case 5. K. D., a 54-year-old housewife, was admitted to the medical service on November 3, 1959, because of dizziness, an unsteady gait, and left-sided weakness which had been present for three days. Three weeks prior to admission she had been treated by her family physician for "the flu." A left simple mastoidectomy had been done 14 years before, and a diagnosis of diabetes mellitus established at that time. Intermittent drainage had occurred from a fistulous tract of the mastoid since that operation.

Examination revealed a well-developed, well-nourished, white female who was unable to give a detailed history because of lethargy and slow speech. Her temperature was 98.6° F., BP 150/80 mm. of hg., pulse 80, and respirations 18. Purulent discharge was present in the left ear canal. There was erythema and tenderness beneath the postauricular mastoidectomy scar. Neurologic examination revealed dysdiadochocinesia on the left. Movements of the left upper extremity were impaired on the finger to nose test, and the patient fell to the left on standing. The deep reflexes were equal but hypoactive.

Laboratory findings included a leucocyte count of 6,650 with 11 per cent stabs and 65 per cent segmented forms. Urinalysis revealed sugar 3+, acetone 3+, and diacetic acid slightly positive. Blood urea-nitrogen was 20 mg. per cent; blood sugar, 408 mg. per cent; chlorides, 90.5 mg. per cent; CO_2, 20.3 volumes per cent; sodium, 137.8 mg. per cent; potassium, 4.7 mg. per cent. Cerebrospinal fluid analysis revealed glucose of 40 mg. per cent; chlorides, 616 mg. per cent; protein 490 mg. per cent; 118,000 WBCs per cu. mm.; 85 per cent neutrophils; and 15 per cent monocytes. Beta hemolytic streptococci group A were isolated on culture of the aural drainage.

Course in hospital: The patient remained afebrile until the third hospital day, when the temperature rose to 103° F. and remained above this level. Consciousness became depressed and neurologic signs increased.

The patient developed slight nuchal rigidity, absence of abdominal reflexes, a left facial paralysis, a left lateral rectus paralysis, and an absent corneal reflex. The spinal fluid pressure was 432 mm. of water. Massive doses of penicillin, erythromycin and chloromycetin were given and Gamma globulin was also given intravenously.

The neurosurgical consultant was of the opinion that a diffuse infectious process was present in the posterior fossa, but that sufficient localization had not yet taken place.

On November 10, 1959, an internist, specialized in antibiotic therapy, evaluated the patient and concluded that response to antibiotics was unsatisfactory. He urged otologic consultation and possible immediate surgical exploration. On consultation, the left mastoid was thought almost certain to be the source of infection of the posterior fossa, and although the patient was comatose and in poor condition, a mastoid exploration was done under local anesthesia. Granulation tissue filled the mastoid antrum and extended over the sigmoid sinus. The sinus wall was thickened, but blood could be aspirated. The posterior fossa dura medial to the sigmoid, as well as the middle fossa dura, appeared normal. No fistulous intracranial extension was found. The patient continued a downhill course following surgery and died the following day.

Necropsy examination revealed the lumen of the sigmoid sinus to be partially filled with a tan granular mass adherent to the endothelium of the sinus. An abscess had developed within the left brachium pontis which was adherent to the petrous bone, dissected into the cerebellum, and ruptured into the fourth ventricle. Culture taken from the abscess cavity revealed B. coli.

COMMENTS.

This patient may very well have been beyond hope of recovery by the time otologic consultation was held. In retrospect, early relief of increased intracranial pressure might have given opportunity to evacuate the posterior fossa abscess before rupture into the fourth ventricle. Again, a Gram-negative antibiotic resistant organism, this time B. Coli, was the cause of the abscess formation.

In the next two cases, both children, a subperiosteal abscess as well as a perisinus abscess was present. In Case 6, the presence of a large cholesteatoma in this three-year-old boy was unsuspected. Both history and clinical findings suggested acute or subacute mastoiditis.

Case 6. R. K., a three-year-old white boy, was admitted March 16, 1960, because of left-sided postauricular swelling gradually developing over a two-week period. A serosanguineous discharge had been present for six weeks and aureomycin had been given. There was a history of an ear infection one year previously, but this was of short duration. There was no subsequent aural discharge or other symptoms of ear disease until six weeks prior to admission.

Examination revealed a temperature of 100° F., pulse 96, and respira-

tions 20. There was a marked postauricular swelling with fluctuation and tenderness. The posterior canal wall was sagging. The tympanic membrane was not completely visible because of the sagging canal and granulation tissue over the pars flaccida. Neurologic examination gave normal findings.

Laboratory findings included a leucocyte count of 16,500 with 72 per cent neutrophils. A culture taken from the ear revealed Proteus vulgaris. Roentgenograms of the mastoids showed diffuse clouding of the left mastoid with cellular destruction. These findings were interpreted as the result of acute mastoiditis.

Course in hospital: After a culture had been taken from the left ear, the patient was started on chloromycetin 250 mg. q.i.d. On March 17, 1960, the day following admission, an endaural mastoidectomy was performed. Upon incising the periosteum, 15 to 20 cc. of thick yellow pus was released. After removing the mastoid cortex, more pus was found surrounding a large cholesteatoma which had eroded the lateral sinus plate. There was a perisinus abscess with a thickened lateral sinus wall and mural thrombus. The lateral sinus was uncovered widely. Cholesteatoma extended into the middle ear and had destroyed the long process of the incus. A tympanostapediopexy was done. The mastoid cavity was not skin grafted. The patient became symptom free and was discharged from the hospital on March 23, 1960. He has remained well.

Case 7. J. S., a nine-year-old white female, was admitted on April 29, 1960, because of a marked left-sided postauricular swelling of two days' duration. Severe pain in the left ear one month previously was followed by a serosanguineous drainage and subsequently a yellow purulent discharge. Her family physician treated her with penicillin and achromycin, which had no apparent beneficial effect on the suppurative process.

Examination revealed a temperature of 102.4° F., pulse 100, respirations 24. The patient was quiet and in no apparent distress. In the left postauricular area there was a very large, tender, fluctuant swelling. A profuse, pulsating, creamy yellow discharge was present in the left ear canal. There was sagging of the posterior-superior canal wall. Secretions taken from the ear canal were sent to the laboratory for culture and sensitivity tests to the common antimicrobial agents.

Laboratory findings included a leucocyte count of 14,900 with 80 per cent neutrophils, 11 per cent lymphocytes, 5 per cent monocytes, 3 per cent stabs, and 1 per cent basal cells. Beta hemolytic streptococci were identified on culture taken from the left ear. Roentgenograms of the mastoids revealed diffuse clouding and cellular destruction of the left mastoid.

Course in hospital: On April 30, 1960, the day after admission, a mastoidectomy was performed through a postauricular incision. Thick, creamy yellow pus was released on incising the periosteum. Again, yellow pus welled forth upon removing the mastoid cortex. The sigmoid plate had been eroded, and the abscess had extended about the sigmoid sinus. Exploration of the sinus wall with a needle revealed marked thickening; however, blood could be aspirated, and, therefore, the vessel was not obliterated. After a complete mastoidectomy, a Penrose drain was placed in the cavity and brought out inferiorly through the incision. While in the hospital the patient was given chloromycetin 0.5 gm. q.i.d. and 600,000 u. of penicillin q.i.d. The patient remained afebrile after surgery and was discharged on May 7, 1960. There have been no further general symptoms. The ear stopped discharging and the hearing soon returned to normal.

Case 8. C. S., a 27-year-old white male, was admitted on July 16, 1952,

because of pain, swelling, and tenderness above the right auricle. This had developed over a three-week period. For three days trismus had been present which produced severe pain while eating. He had had intermittent drainage from the right ear for four or five years. A simple and a modified radical mastoidectomy had been performed in the past.

Examination on admission revealed an alert patient who appeared to be in pain. His temperature was 102.2° F., pulse 92, and respirations 22. There was marked tenderness, swelling, and fluctuation above and in front of the right auricle. Purulent drainage was present in the ear canal from which a culture was taken. Swelling obscured adequate visualization of the tympanic membrane. There was a fistulous tract into the mastoid cavity with purulent drainage.

Laboratory findings included a leucocyte count of 8,150 with 61 per cent neutrophils and 39 per cent lymphocytes. Roentgenograms showed a bony defect 2 cm. by 2 cm. in the squamous portion of the temporal bone and another 1 cm. by 1 cm. in diameter above the zygomatic root. Culture was taken from the ear and showed Aerobacter aerogenes.

Course in the hospital: Prior to return of the culture report, the patient was placed on penicillin 600,000 u. q.i.d. and achromycin 250 mg. q.i.d. Subsequently, dihydrostreptomycin 0.5 gm. b.i.d. was added. On the day after admission the mastoid cavity was explored. Cholesteatoma was found as the fistulous tract was followed to the dura. The lateral sinus plate had been eroded and a perisinus abscess was present as well as a mural thrombus of the sigmoid portion of the lateral sinus. After completion of a radical mastoidectomy and removal of cholesteatoma and granulations from the middle ear, an epidural abscess was found over the temporal lobe. Cholesteatoma extended over an area 2 cm. by 3 cm. above the mastoid. A similar cholesteatomatous mass was present above the zygomatic root. Cholesteatoma was meticulously stripped from the dura. This resulted in a small dural tear with leakage of spinal fluid which was readily controlled with gelfoam sponge and pressure. Following surgery, the temperature gradually returned to normal. The patient was discharged after ten days, but antibiotic therapy continued for another three weeks.

COMMENTS.

The unusual feature of the above case was the very marked extension of cholesteatoma beyond the confines of the temporal bone over the lateral sinus and middle fossa dura. The dura apparently acted as an effective barrier to the epidural infection and prevented invasion of the underlying brain.

Case 9. M. W., a 39-year-old white female, was admitted September 27, 1956, because of right facial paralysis. This had developed slowly over an eight-year period, but had become almost complete one year before admission. Intermittent vertigo and diplopia had been present for six months. There had been increasing unsteadiness with movement. The left ear had been discharging intermittently since scarlet fever in childhood.

Examination on admission revealed a temperature of 98.8° F., pulse 84, and respirations 16. The patient appeared to be in no acute distress while at rest. The right side of the face was almost completely paralyzed with only a flicker of motion remaining. The right tympanic membrane

had been destroyed, and the middle ear was filled with a chalky white, dry cholesteatoma. The fistula test was positive. The hearing by bone conduction remained. The remaining neurologic examination gave negative findings.

Laboratory findings revealed a leucocyte count of 9,800 with 60 per cent neutrophils. Culture of the right ear obtained Proteus vulgaris. Roentgen examination revealed a large radiolucent area involving the entire mastoid bone, throwing the semicircular canals into unusual relief throughout the radiolucent area.

Course in hospital: The patient was started on chloromycetin. An endaural radical mastoidectomy was performed on October 1, 1956. The entire mastoid cavity was filled with a huge cholesteatoma, and the bony plate over the sigmoid sinus and jugular bulb had been eroded. Pus surrounded the vessel, and there was marked thickening of the wall. The cholesteatoma matrix was adherent to the horizontal semicircular canal and had produced a fistula. The Fallopian canal had been destroyed, and the nerve was surrounded by cholesteatoma from the geniculate ganglion to the stylomastoid foramen. The matrix was carefully stripped and teased away from the nerve. Granulation tissue and cholesteatoma were removed from the middle ear. Three weeks following surgery, muscles supplied by the mandibular branch of the facial nerve began to function. After nine months, all muscles of facial expression functioned well with only a very slight remaining weakness of action.

Case 10. E. S., a 74-year-old white male, was admitted on June 24, 1958, in a confused state after he had collapsed at home the morning of admission. The patient was known to have had a marked hearing loss and to have had intervals of imbalance, but none just prior to his present illness.

Examination on admission revealed a temperature of 97.4° F., pulse 86, and respirations 26. The patient was in a state of confusion. The left tympanic membrane was scarred, and there was a calcification of the right tympanic membrane, a posterior marginal perforation, and a scanty purulent discharge. Smears and culture of this exudate were taken.

Laboratory findings included a leucocyte count of 10,350 with 89 per cent segmented neutrophils, 5 per cent stabs, and 6 per cent lymphocytes. A lumbar puncture obtained normal pressures. This fluid contained no leucocytes, 163 erythrocytes per cu. mm., protein of 159.9 mg. per 100 ml., sugar 22 mg. per 100 ml., and chlorides 113 mEq. per liter. Chest and sinus X-rays showed normal findings. There was diffuse sclerosis of both mastoids. Blood culture showed no bacterial growths. Culture from the right ear revealed Aerobacter aerogenes.

Course in hospital: From the time of admission, diurnal fluctuations of temperature ranged from 98° F. to 106° F. He was given chloromycetin, erythromycin, and aureomycin, intravenously and in combination, varying from one-half to one and one-half grams daily of each drug. When the patient became comatose on June 28, 1958, a neurosurgical consultation was obtained. There was marked tenderness at the base of the skull and bilaterally in the suboccipital region. A thrombosis of the lateral dural sinus was suspected and otologic evaluation requested. A spinal puncture was done with manometric recordings following jugular compression, and the Tobey-Ayer test was found to be positive. A complete mastoidectomy was performed on July 15, 1958. Hemorrhagic mastoiditis extended to the lateral sinus. There was a perisinus abscess and complete thrombosis of the vessel. The infected thrombus was removed from the jugular bulb to the torcular Herophili. The jugular vein was ligated in the neck, since an infected clot remained in the

jugular bulb and free bleeding could not be obtained. The post-surgical course was that of temporary improvement. The patient was more alert, and his temperature remained normal. Six days following surgery the temperature again became elevated in spite of continued intensive antibiotic therapy. He continued on a downhill course and died on July 29, 1958. Autopsy revealed a brain free of focal inflammation, abscess formation, or generalized meningitis. The obliterated right dural venous sinus showed early organization. Cerebral arteriosclerosis was present, and there was evidence of a cerebellar pressure cone.

COMMENTS.

In this case a septic thrombus extended from the torcular Herophili to the jugular vein in the neck. Jugular vein ligation seemed indicated in this case, since the thrombus was obviously infected and extended beyond the jugular bulb. The Gram-Negative bacillus, Aerobacter aerogenes, proved resistant to massive intravenous antibiotic therapy.

DISCUSSION.

The infections encountered all showed considerable resistance to antibiotic therapy. With the widespread use of antibiotic and chemotherapeutic agents, profound changes in the character of infections have taken place. In seven of the above cases, infection was produced by Gram-negative organisms of the coliform group, bacteria commonly found in chronically discharging ears. Finland, *et al.*,[22] have been impressed by the increased prevalence and seriousness of infections produced by these organisms. Colon bacilli, widely prevalent and often considered benign in the past, now frequently become pathogenic, invasive microorganisms which respond poorly to antimicrobial agents. Through mutation and selection, microorganisms evolve which are antibiotic-resistant.

Thorough consideration of all knowledge of our present antimicrobial agents and the organisms they are designed to affect must be utilized. In the future, perhaps new discoveries will be made to overcome the changes produced by bacteria in the host and his total bacterial flora and methods found to increase resistance against bacterial infections in general. At present, the use of massive doses of antibiotics should reduce the numbers of bacteria which by mutation could

develop resistance. The use of two antibiotics in combination makes resistance to both of them less likely, since this would require mutation of two independent characters.[33] Smears and cultures to identify the specific causative agent should be taken before instituting treatment. Knowledge of the statistical effectiveness of the various groups of antibiotics on the species of infecting organisms in question should be used. This information, as suggested by Dolowitz, *et al.*,[34] should be used along with the results of the sensitivity studies of the bacterial culture. Better therapeutic effects should be obtained as a result. If, however, by clinical evaluation the therapeutic response is not satisfactory, the antimicrobial agent must be changed.

The above experience points out the ineffectiveness of our present antimicrobial agents on certain bacterial infections within the temporal bone. The otologist must continue to be alert to the possibility of a retained focus of infection in the petrous apex and to the possibility of intracranial spread of infection through venous channels. As has been shown, the symptoms and signs of these infections often do not follow the classical patterns described in the preantibiotic era. Diseased bone still must be removed, and pus must be drained if a disastrous outcome is to be prevented.

SUMMARY.

There is an increasing occurrence of infections which are resistant to chemotherapeutic and antibiotic agents. Bacterial organisms, often found in chronically discharging ears and considered benign in the past, now frequently become pathogenic and invasive.

Infection was resistant to antibiotic therapy in the ten cases of mastoid complications studied. Gram-negative bacilli of the coliform group were the causative organisms in seven cases.

Three cases of petrositis with intracranial extension of infection recovered only after surgical removal of infection from the petrous apex.

Lateral sinus thrombosis was encountered in seven cases. In two instances this led to the formation of a cerebellar abscess. Other complications accompanied the lateral sinus infections. These were two subperiosteal abscesses, an epidural abscess, a facial paralysis, and a labyrinthine fistula.

Antimicrobial agents used in massive doses and in combination may effect a partial response and delay dissemination of the infection; nevertheless, foci of infection may remain deep in the temporal bone or the brain and become manifest at a later date.

The otologist must be alert to altered clinical patterns in patients treated with antibiotics which indicate remaining infection within the temporal bone or early invasion of the venous channels.

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NEW YORK EYE AND EAR INFIRMARY ALUMNI MEETING.

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Additional information may be obtained by writing to Dr. Merrill Goodman, Secretary, Alumni Association, 218 Second Avenue, New York 3, N. Y.

A CLINICAL EVALUATION OF CALORIC TESTING BY THE FITZGERALD-HALLPIKE-CAWTHORNE METHOD.*

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Tests of labyrinthine function, whether caloric, faradic, or rotational, do not approach the degree of accuracy provided by the more refined audiometric tests. The localization of lesions affecting the vestibular apparatus is uncertain, largely because the central connections of the system are incompletely understood, but also because ordinary labyrinthine tests fail to provide information other than whether or not the labyrinth functions.

Interest in the possibilities of hot and cold caloric testing for localizing central lesions was first aroused by de Barenne and de Kleyn in 1923.[1] In attempting to confirm the results of Bauer and Leidler[2] who reported in 1911 that, following removal of one cerebral hemisphere in the rabbit, cessation of rotation caused a much brisker response toward the side of the intact hemisphere, de Barenne and de Kleyn obtained similar results on warm caloric testing; but on testing with cold water, they noted that the opposite labyrinth was the more irritable. They observed that the nystagmus induced both by warm and cold testing lasted longer toward the side of the absent hemisphere, no matter which ear was tested. They postulated that extirpation of one cerebral hemisphere gave a central facilitation of induced nystagmus in the direction of the lesion.

De Kleyn and Versteegh in 1927 examined 36 patients by the hot and cold caloric method, using the Kobrak technique

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of graded stimuli. Eleven showed a prolonged response of nystagmus in one direction, and one of these proved to have a frontal lobe abscess on that side; however, it remained for Fitzgerald, Hallpike and Cawthorne to define a technique utilizing hot and cold caloric testing to localize central lesions. Their method is as follows: the patient is placed supine with the head flexed 30 degrees, and each ear is douched in turn with water at 30 degrees C. and 44 degrees C. (7 degrees below and above body temperature). The douche can is suspended about two feet above the patient's head, and the nozzle through which the water is delivered into the external auditory meatus has a 4 mm. bore. The douching is continued for 40 seconds. At least five minutes should be allowed between tests to allow the patient to recover.

The induced nystagmus is timed from the beginning of the douche: only second degree nystagmus is considered significant. Duration of nystagmus is recorded on a chart which allows one to tell at a glance whether directional preponderance of nystagmus, hypoactivity of one labyrinth as compared with the other (canal paresis), or a normal caloric pattern is present (see Fig. 1). Normally, nystagmus lasts 50 to 180 seconds; 40 seconds' difference between the sum of the two longer reactions and of the two shorter reactions is considered significant of a directional preponderance of nystagmus or of canal paresis.

Fitzgerald and Hallpike's first report[3] revealed that directional preponderance of nystagmus was present to the side of the lesion in all of ten cases of temporal lobe lesions, and that in ten other cerebral lesions caloric tests were normal. They concluded that tonic controlling centres exist in the temporal lobes, exercising their effect upon the reflex responses of the lower vestibular centres through corticofugal fibres.

In their next paper, Fitzgerald and Hallpike with Cawthorne[4] studied the vestibular responses of 138 patients with Ménière's disease: most of these showed so-called canal paresis. Nine patients underwent labyrinthectomy following which all nine showed directional preponderance to the oper-

ated side. Thus, tonic vestibular as well as cortical impulses were apparently involved in the production of vestibular nystagmus.

In the third paper by the same authors,[5] tests on 50 patients with Ménière's disease showed 29 cases of canal paresis, ten cases of directional preponderance to the opposite side, and

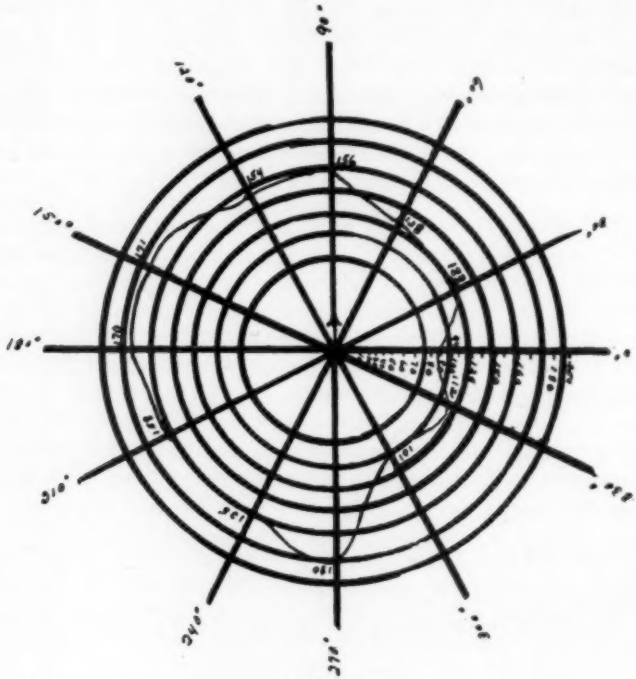

Fig. 1.

some combinations. They postulated that an utricular paresis can give directional preponderance to the opposite side.

On reviewing the Fitzgerald-Hallpike-Cawthorne caloric test, it is seen that alternate warm and cold testing may reveal diminished response in one ear termed canal paresis, or may show prolonged nystagmus in one direction no matter

which ear is tested. This directional preponderance of nystagmus, according to the authors, indicates a temporal lobe lesion on the side to which nystagmus is of longest duration, or an utricular lesion on the opposite side.

Various opinions have been published concerning the value of the Fitzgerald-Hallpike-Cawthorne method of vestibular testing. Jongkees[6] in 1948 reported testing 125 normal subjects and found directional preponderance in 17 per cent and dominance of one labyrinth in 5 per cent. He concluded that the test has restricted value in that it may indicate apparently normal, subnormal or destroyed function of one labyrinth.

On the other hand, Hoople[7] in 1949 commented that, in conjunction with allied examinations and a good history, the findings of this test seem more conclusive than those elicited by other caloric tests. Hallpike, Harrison and Slater[8] in 1951 tested 93 normal subjects and found no significant percentage of either directional preponderance or of canal paresis. In 35 cases of severe anxiety neurosis, a greater over-all sensitivity as shown by longer duration of nystagmus and a greater degree of variance, were reported.

In 1953 Permin[9] tested 83 patients with "labyrinthosis". In 43 cases showing directional preponderance, a hearing impairment was correlated in only seven; in 12, hearing impairment was on the unaffected side, and in 24 cases hearing was normal or equally affected in both ears. In 25 cases of canal paresis, hearing was impaired in the affected ear in 11; in the unaffected ear in only two, and was equally impaired or normal in 12. He concluded that the Fitzgerald-Hallpike-Cawthorne test appears to yield no more information than does determination of spontaneous and postrotatory nystagmus.

Petermann[10] in the same year reported finding directional preponderance in only one of 100 normal test cases. He stated that directional preponderance appears to be a pathological sign, and also that caloric labyrinthine reactions are influenced by general functional disturbances.

Thomsen[11] was somewhat more critical. On testing 50 normal subjects he demonstrated a total left preponderance of 38.3 seconds and total right preponderance of 30.9 seconds in 95 per cent. His conclusion was that if the limit or normality is 40 seconds, then values for normal and abnormal may fall together within a given range.

Carmichael, Dix and Hallpike[12] in 1954 reported that directional preponderance of caloric and optokinetic nystagmus was absent in frontal lobe lesions, in the upper half of parietal lobe lesions, and in the anterior portion of temporal lobe lesions. Directional preponderance toward the side of the lesion was consistently present in patients with a lesion limited to the posterior half of the temporal lobe or involving the area of the supramarginal and angular gyri on the same side.

A somewhat conflicting report was published in the same year by Kirstein and Preber.[13] They compared electroencephalographic findings with directional preponderance in 68 patients with cerebral disorders. Directional preponderance occurred in 29, and in 25 of these, EEG showed a focal abnormality in the frontal, temporal, or parieto-occipital regions. In eight cases with normal calorics a focal abnormality was recorded from either the frontal or temporal region. They concluded that directional preponderance in cases with cerebral lesions has no unequivocal localizing value and that the absence of directional preponderance does not exclude a lesion of either the frontal or temporal region.

In 1954 Andersen[14] reported testing 30 normals and 50 extracranial lesions: these did not show directional preponderance to any extent. Fifty-five supratentorial lesions were also tested, 21 of which showed directional preponderance, 19 to the affected side. In unilateral space-occupying lesions, 17 of 46 showed directional preponderance. Directional preponderance was also found in some cases of multiple sclerosis, epilepsy, sequelae of head injuries, and Ménière's disease. He stated that it seems an affection of the temporal lobe is not invariably associated with directional preponderance, and

directional preponderance may occur in the absence of temporal lobe involvement.

In testing 225 cases of Ménière's disease, Harrison[15] in 1955 found unilateral abnormalities in 83 per cent. Of these, 50 per cent showed canal paresis and 20 per cent showed directional preponderance to the opposite side. Hearing loss and tinnitus were frequently found on the opposite side.

Sandberg and Zilstorff-Pedersen[16] in 1960 tested 35 patients with temporal lobe lesions confirmed later at operation. They found that of 11 lesions in the posterior part of the temporal lobe, directional preponderance occurred in ten. In anterior temporal lobe lesions, six of 13 showed directional preponderance, and in lesions involving both parts, five of 11 showed directional preponderance.

It is evident that some disagreement exists as to the value of the Fitzgerald-Hallpike-Cawthorne test, and we decided to investigate it clinically before we condoned or condemned it.

It would seem that the practicability of a clinical test depends not only upon its giving certain results in the great majority of cases for which it is specific, but also on its being more or less confined to these cases. Other signs and symptoms also should show consistently an association with such a test.

Some of the previously quoted publications have shown that directional preponderance occurs with temporal lobe lesions and utricular lesions in many cases. Our study is an endeavour to determine whether directional preponderance and canal paresis occur in a significant number of inner ear or Central Nervous System lesions, and, if so, whether they are correlated with the other signs of the lesion.

Cases selected for testing were patients complaining of vertigo or of hearing loss which could not be explained by audiometric testing alone and in which some vestibular or central element was suspected. One hundred such patients were subjected to routine examination of the ears, nose, and throat, and audiometric testing with such special tests as

were indicated. After the patients were examined for evidence of spontaneous nystagmus, past-pointing and dysdiadochocinesia, Romberg, finger-to-nose and heel-shin tests were performed. An attempt was made to elicit positional nystagmus, then the Fitzgerald-Hallpike-Cawthorne test was done, and the results were recorded in the usual fashion. The complete record of each patient was reviewed six months to one year later in order to find the results of all other examinations and the final diagnosis.

Out of the 100 cases, 24 showed a directional preponderance of nystagmus. In 16 of these cases the hearing was normal or impaired equally in each ear. In five cases the hearing was impaired in the unaffected ear or the ear opposite that which one would expect on the basis of utricular paresis or intracranial pathology. In only three cases directional preponderance agreed with the measured hearing loss. Twelve cases were associated with true vertigo; other symptoms were inconstant. The diagnoses included seven cases of basilar artery insufficiency, three convulsive disorders, two presbycusis, three conversion hysteria, two Ménière's disease, two multiple sclerosis, and single cases of kanamycin sensitivity, leptomeningeal sarcoma of the posterior cranial fossa, positional syncope, and parietal cerebral thrombosis. One case had no diagnosis.

Thirty-three of the tests showed canal paresis, with hearing impairment in the affected ear in 23, in the unaffected ear in four, and with normal or symmetrically impaired hearing in six. True vertigo was present in 16 and tinnitus in 15: other signs and symptoms were inconstant. The diagnoses included endolymphatic hydrops 11 cases, vascular insufficiency seven, cochlear vascular accident four, presbycusis two, psychoneurosis two, old head injury with possible temporal bone fracture two, and single cases of herpes zoster oticus, multiple sclerosis, acoustic neurinoma, streptomycin toxicity, and multiple myeloma metastatic to the base of the skull (see Fig. 2).

Considering the test from the patients' viewpoint, it was generally well tolerated. There were a few cases of mild

nausea during the testing, but no vomiting occurred, and many of the patients tested who had had previous ice water caloric tests remarked on the absence of unpleasant sensations. One patient stated that the test had eliminated her dizziness: this was not expected to be a permanent cure.

The tests were somewhat time-consuming, however, the average time being 25 minutes: this represents a considerable

100 Patients with Otological or Neurological Symptoms.

Reaction of Patient	Canal Paresis (33)		Directional Preponderance (24)	
Hearing Impaired in Affected Ear	23		3	
Hearing Impaired in Unaffected Ear	4		5	
Hearing Normal or Equally Impaired in Both Ears	6		16	
Diagnoses	Endolymphatic Hydrops	11	Basilar Artery Insufficiency	7
	Vascular Insufficiency	7	Convulsive Disorders	3
	Cochlear Vascular Accident	4	Conversion Hysteria	3
	Presbycusis	2	Presbycusis	2
	Psychoneurosis	2	Ménière's Disease	2
	Head Injury with Possible Temporal Bone Fracture	2	Multiple Sclerosis	2
			Kanamycin Sensitivity	1
			Leptomeningeal Sarcoma of Posterior Fossa	1
	Herpes Zoster Oticus	1	Positional Syncope	1
	Multiple Sclerosis	1	Parietal Cerebral Thrombosis	1
	Acoustic Neurinoma	1	No Diagnosis	1
	Streptomycin Toxicity	1		
	Multiple Myeloma Metastatic to Skull Base	1		

Fig. 2.

amount of time for one procedure in the office of an otolaryngologist, and detracts considerably from the practicability of the test.

In our opinion, the chief liability of the test was the appearance of directional preponderance in such a variety of lesions and its lack of correlation with the other signs, particularly hearing loss. Even though it appears with certain temporal lobe lesions, the fact that it may also be found in a variety

of common otological and neurological lesions without relation to other established findings lessens its value as a diagnostic test.

Canal paresis, on the other hand, was correlated with other signs in the vast majority of cases. It must be pointed out that a simple cold caloric test would have yielded the same result. A possible advantage of the Fitzgerald-Hallpike-Cawthorne test is that the alternate hot and cold caloric tests may provide a more accurate quantitative appraisal of the function of one labyrinth in comparison with the other.

SUMMARY.

A review of the origin and development of the Fitzgerald-Hallpike-Cawthorne method of vestibular testing is given. Opinions have been published both for and against the claims of the originators. In testing 100 cases of otological and neurological lesions by this method, the finding of canal paresis was significant in most cases. Directional preponderance of nystagmus was found in a variety of lesions and was poorly correlated with other signs: its significance as being diagnostic of a certain lesion is doubtful.

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The next meetings of the American Society of Facial Plastic Surgery will be held on January 19, 1962, at the Hotel Elysee, 60 East 54th Street, New York, N. Y., and on March 3rd through March 5th at the Hotel Roosevelt, New Orleans, La. For further information address Samuel M. Bloom, M.D., Secretary, 123 East 83rd, New York 28, N. Y.

AFFERENT IMPULSES IN THE RECURRENT LARYNGEAL NERVE IN THE CAT.*

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INTRODUCTION.

It is generally believed that the recurrent laryngeal nerve carries only the efferent or motor impulses to the intrinsic muscles of the larynx; however, the existence of afferent fibers was already suggested by Burkart[2] (1868), who observed respiratory changes by giving electrical stimuli to the central end of a severed recurrent nerve in the rabbit. Schultz and Dorendorf[18] also reported that electrical stimulation given to the recurrent nerve was followed by a transient increase in blood pressure and decrease in frequency of respiration in the rabbit, dog and cat. They stated that these changes are reflectingly elicited by stimulation ascending along the afferent fibers of the recurrent laryngeal nerve.

Murtagh[14] examined the effect of Faradic current stimulation of the central end of the cut recurrent nerve. In his experiment on the goat recurrent nerve, there was no evidence of reflex changes following stimulation; therefore, he assumed that there are no afferent fibers in the recurrent laryngeal nerve. Later, Murtagh and Campbell[15] noted respiratory arrest as a result of high intensity stimulation of the recurrent nerve in the goat. They considered the effect might be due to electrical spread or escape of stimulus to the vagus itself.

From the anatomical standpoint, Broeckaert reported that the human recurrent nerve is a mixed nerve carrying motor fibers to the larynx, and motor and sensory fibers to the esophagus and trachea. Brocklehurst and Edgeworth[1] con-

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sidered that the recurrent nerve consisted of two components: laryngeal and sensory. They showed that about one third of the nerve fibers up to 8.5 μ in diameter remain undegenerated after section of the vagus, at levels central to the jugular or to the nodose ganglion. Many of these fibers were observed to run to the trachea and esophagus, and the few remaining at laryngeal level become continuous with a branch from the superior laryngeal nerve. They stated that about 3 per cent of the myelinated fibers remaining at the laryngeal level are considered to be proprioceptive sensory.

Lemere[12] demonstrated in the dog that the recurrent nerve is divided into two branches: one of which is of a sensory nature distributed in the trachea, esophagus and subglottic space. He designated the branch as the pararecurrens. More recently, Williams reported that the human recurrent nerve sends at least 12 branches to the trachea and esophagus in the cervical region and finally reaches the larynx in two bundles.

The function of the fiber groups in the recurrent laryngeal nerve, especially that of the afferent component, has long been a subject of many investigators, and the problem has not yet been completely solved. For this reason, the present author made a fundamental study on the unsolved points concerned.

METHODS.

Healthy adult cats ranging in weight from 2 to 4 Kg. were anesthetized with intraperitoneal Nembutal—dosage 15 mg. per Kg. body weight. A venous cannula was inserted for further control of anesthetic condition and additional administration. Each animal anesthetized was placed on a stereotaxic apparatus. The mouths were kept open by gags during experiment. A median cervical incision was performed to approach the larynx and trachea. In the peritracheal connective tissues, the recurrent laryngeal nerve was readily observed running along the trachea. Special attention was paid in this study to preserving the recurrent laryngeal nerve intact. For this purpose, the peritracheal connective tissues containing

the recurrent nerve were gently separated from the trachea and laterally reflected. The trachea was severed after complete exposure and freed from surrounding tissues. A tracheal cannule was inserted into the lower end of the cut trachea, while the upper end was elevated and slightly reflected to the larynx. The wound thus prepared was filled with liquid paraffine to enable clear visibility of the recurrent nerve in the paraffine pool. The connective tissues around the nerve were then removed together with the perineurium itself as well as possible by using sharp needles under a binocular operation microscope. Direct injury to the nerve was strictly avoided.

Fig. 1. Spontaneous afferent impulses in the recurrent laryngeal nerve in the cat.

The nerve enters the larynx on its upper edge at the posterior surface of the larynx. At this point, small blood vessels also enter the larynx and, therefore, no attempt was made to clean the nerve in this region.

The exposed nerve with a length of about 1.5 cm. from the larynx was then severed and placed on a leading electrode. A bipolar silver electrode was used in this experiment. Recording was undertaken by a double-beam cathode-ray oscillograph and a long recording camera in the usual manner.

RESULTS.

It was found that there was a continuous afferent discharge from the larynx when the recurrent laryngeal nerve was severed and the peripheral (laryngeal) end put on the leading electrode. If the removal of the perineural connective tissues was sufficient, the afferent impulses recorded were considered to come from a single unit on the usual criteria, that is to say, the action potentials were of constant height and formed part of a regular rhythmic series. The rate of

discharge varied from 10 to 110 impulses per sec. Figure 1 shows a record of afferent impulses from a single unit. The impulse frequency shows approximately 10 impulses per sec.

The frequency of afferent impulses was observed to remain almost unchanged even after the recurrent nerve of the opposite side and superior laryngeal nerves of both sides were severed; also, no remarkable effect of respiratory movement was observed on discharge frequency (see Fig. 2).

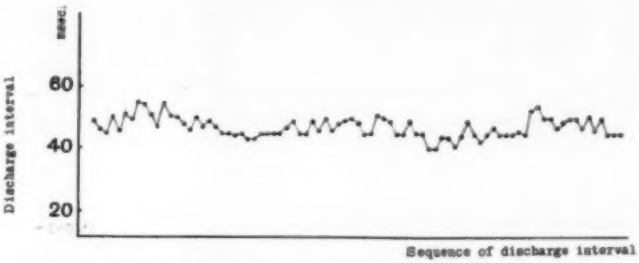

Fig. 2. Interval diagram of spontaneous afferent impulses in the recurrent laryngeal nerve.

Fig. 3. Effect of extension of the larynx upon discharge frequency of afferent impulses in the recurrent nerve.

An extension of laryngeal lumen obtained by a lever inserted into the larynx through the mouth produced a marked acceleration of the afferent impulses, and usually no other new units were recognized (see Fig. 3). The acceleration continued while the extension was maintained. The pattern of response shown in the frequency diagram was of a slowly adapting nature (see Fig. 4). The rate of discharge decreased and returned to its original level when the extension was released. Figure 5 shows the interval diagram of the same record. In this case, the rate of discharge immediately rose

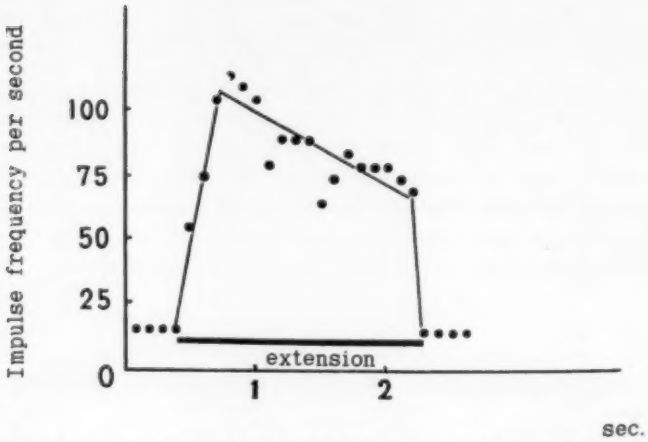

Fig. 4. Diagram of impulse frequency, indicating the effect of extension of the larynx upon discharge frequency.

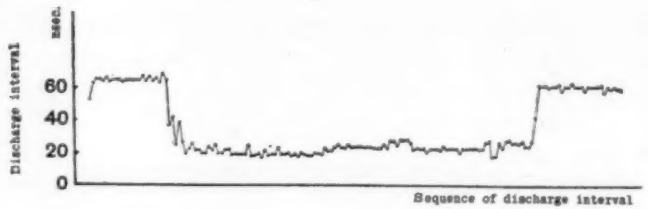

Fig. 5. Interval diagram, indicating the effect of extension of the larynx upon discharge.

to approximately 110 impulses per sec., which, after a short burst, settled to roughly 75 impulses per sec.

Moderate pressure was applied to the anterior surface of the larynx in order to release the tension of the laryngeal muscles. As a result, the rate of discharge dropped below the original level and remained almost constant during pressure. Figure 6 shows the effect of pressure of the afferent impulses in the recurrent nerve. This pattern is also illustrated in Figures 7 and 8.

Fig. 6. Effect of pressure on the larynx upon discharge frequency of afferent impulses in the recurrent nerve.

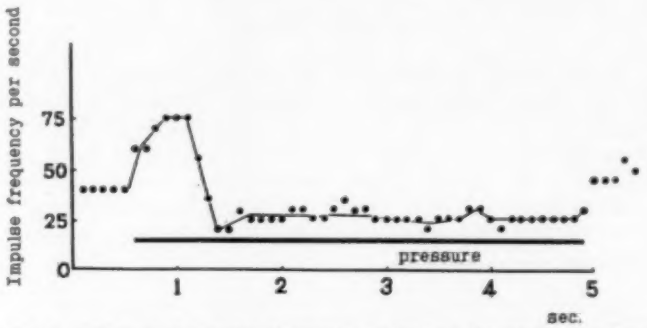

Fig. 7. Diagram of impulse frequency, indicating the effect of pressure on the larynx upon discharge frequency.

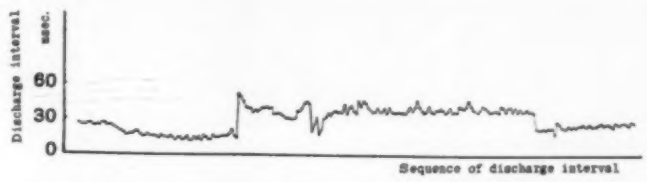

Fig. 8. Interval diagram, indicating the effect of pressure on the larynx upon discharge.

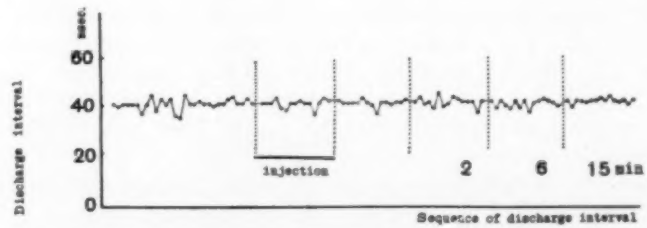

Fig. 9. Interval diagram, indicating the effect of Decamethonium given 0.05 mg. per Kg. body weight intravenously. No remarkable changes are recognized in discharge interval immediately, 2, 6 and 15 minutes after the injection.

Further experiments were made in which the animals were injected intravenously with 0.05 mg. (per Kg. body weight) of Syncurine (Decamethonium bromide) under artificial respiration. As shown in Figure 9, continuous recording revealed no remarkable change in the rate of discharge.

CONSIDERATIONS.

In the present experiment, it was electrophysiologically proven that there are afferent components in the recurrent laryngeal nerve in the cat. The afferent impulses recorded from the recurrent nerve were considered to come from nerve endings in the larynx, since the recording was always made at the peripheral (laryngeal) end of the severed nerve, and this should have reduced the influence of tracheal and esophageal components.

It should be necessary to determine the nature of the nerve endings, although the aim of the present study was to establish the presence or absence of afferent discharge in the recurrent laryngeal nerve rather than to provide a detailed quantitive account of its activity. In other words, it must be determined whether the afferent discharge originated from muscle spindles in the laryngeal muscles, since the afferent impulses recorded were slowly adapting in the pattern of response to both extension and pressure applied to the larynx.

There has been a considerable number of papers on the problem of proprioception of the larynx. As for the fiber distribution of the muscle nerve, Eccles and Sherrington[6] reported that the fiber spectrum of many skeletal muscles shows two peaks, one at about 6 μ and the other in the neighborhood of 15μ. In 1951, Fernand and Young[7] examined a wide range of muscle nerves and classified their fiber spectra as unimodal —single peak; and bimodal—two peak. They stated that the bimodal nerves contain many large fibers of 14 to 20 μ in diameter, a few fibers in the 10 to 20 μ range and smaller fibers with a mode of 6 to 8 μ, and that this type of fiber distribution is found mainly in the limb muscles. They revealed also that the unimodal muscle nerve does not contain large fibers and considered that the recurrent nerve belongs

to the group of unimodal muscle nerves. Murray also studied the fiber distribution of the recurrent nerve in the cat and concluded that the recurrent nerve consists of fibers ranging in diameter from 10 to 12 μ and shows unimodal distribution.

More recently, Murtagh and Campbell[16] reported that all the histograms of the recurrent nerve of man, goat and cat are unimodal.

From the foregoing, it is reasonable to consider that the recurrent nerve is unimodal in fiber distribution and that there is a considerable difference in this respect between the recurrent nerve and other nerves innervating limb muscles.

As for the two peaks in the fiber spectra of motor nerves, it has been widely accepted that large efferent fibers are responsible for muscle contraction and the small fiber group which is referred to as gamma (γ) fibers, innervates the intrafusal fiber in muscle spindle, while the spindle afferent fibers are contained in the large fiber group. Since the recurrent laryngeal nerve was found to be unimodal in fiber distribution, it has been suggested that the recurrent nerve contains neither gamma nor proprioceptive fibers. Fernand and Young[7] specifically stated that they had definite evidence to account for the absence of afferent fibers in the recurrent laryngeal nerve.

It is generally believed that mammalian laryngeal muscles are devoid of muscle spindles; however, the finding of muscle spindle in the laryngeal muscles in man or monkey has been reported by several authors, among them were Brocklehurst and Edgeworth,[1] Sugano and Paulsen. Recently, Keene[11] stated that there are "numerous" spindles in human laryngeal muscles.

From physiological standpoints, Murtagh and Campbell[16] observed the action potentials and conduction velocity of the recurrent nerve in the goat and concluded that it contains gamma fibers. They also suggested there might be a proprioceptive supply from the laryngeal muscles in the goat.

Concerning the activity of muscle spindle, it was reported

by Granit, *et al.*,[9] that muscle spindle is markedly activated by intravenous injection of Decamethonium solution. This view was confirmed by other investigators, though the mechanism of activation has not yet been thoroughly clarified.

In the present experiment, Syncurine, 0.1 per cent isotonic Decamethonium bromide, was intravenously administrated, and the response in discharge pattern was observed. As a result, there was no remarkable change in frequency of afferent impulses following administration. This fact would indicate that the afferent discharge recorded in the present experiment did not originate from muscle spindles in the laryngeal muscles.

Although the author has no definite opinion concerning the origin of the discharge, it possibly comes from a kind of pressoreceptor of a slowly adapting nature in the fascia or other connective tissues in the larynx. Further histological examination must be made in order to clarify a more exact origin of the discharge.

SUMMARY.

It was electrophysiologically proven that there are afferent components in the recurrent laryngeal nerve in the cat.

It was assumed that the afferent discharge recorded did not come from muscle spindles, judging from the pattern of response to intravenous administration of Decamethonium solution.

The afferent discharge probably comes from a kind of pressoreceptor of slowly adapting nature existing in the fascia or other connective tissues in the larynx.

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COURSE IN OTOLARYNGOLOGY.

A medical continuation course, Otolaryngology for Specialists, will be presented at the Center for Continuation Study, University of Minnesota, Minneapolis, Minnesota, January 25-27, 1962. For further information address W. Albert Sullivan, Jr., M.D., Director, 1342 Mayo Memorial, Minneapolis 14, Minn.

CANCER OF THE NASOPHARYNX:

With Special Reference to the Significance of Histopathology.*

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Cancer of the nasopharynx has aroused a lively interest in recent years. Malignant disease of this space is unique in many ways: the nasopharynx is hidden from the average observer by the palatine curtain; its location under the base of the skull is strategic; and many surrounding structures are affected by neoplastic invasion.

The onset is insidious and, during the early phase, may give rise to few or no alerting symptoms. The general well-being of the patient belies the sinister import of the tumor. Results in the past have been so discouraging that physicians have been imbued with a sense of futility. The prognosis has been improved with the recent advances in the technique of radiotherapy. As the medical profession has become more aware of this disease, the reported incidence has increased progressively.

In this paper the clinical picture will be developed from an analysis of 57 cases, and the significance of the histopathology will be evaluated.

HISTORICAL NOTES.

Baranger[1] reviewed the literature and found that Durand-Fardel (1837) was the first to report the finding of malignant tumor in the nasopharynx at autopsy. Godtfredsen[2] cited this fact, but noted that the tumor may have been an extension into the nasopharynx from the nasal cavity;

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however, he listed the following: Michaux (1845), first nasopharyngeal carcinoma verified histologically; Lotzbeck (1859), first case verified by autopsy; Schweich (1867), first case of nasopharyngeal sarcoma; and Flour (1873), first case with neural symptoms. Other reports by Veillon (1874), Hallade (1880), Mühlfarth (1893), Monboyran (1895) and d'Escat (1901) followed.

Baranger[1] noted further that d'Escat's was the first definitive clinical report of this lesion. He listed, in addition, the following authors: in France, Aboulker, d'Alger, Pauliac (1911), Sargnon, Jacod (1915, 1921); in Germany, d'Heymann (1890), Wasserman (1896), Schreiber (1896), Platau (1897) and Oppikofer (1913); in Italy, Moncalli (1893), Citelli (1902), Castellani (1911); in Spain, Compayred (1905); in England, Symmonds (1896), Trotter[3] (1911); and in America, Jackson[4] (1901), Howes (1903) and Rhodes (1907). Baranger deplored the difficulties in making an early diagnosis, and the failures of treatment with X-ray and radium in the advanced cases; an observation with which all authors have agreed. The duration of the disease in Baranger's experience averaged between one and two years.

Godtfredsen[2] cited the contributions of the following authors: Laval (1904), who classified the disease in respiratory, auricular, and cervical glandular forms. He noted that the disease had a latent period of vague symptoms from a few months to six or seven years; a manifest period with pains in the pharynx and ears, and an invasive period with local metastases. Laval and his contemporaries employed surgery with completely unsuccessful results. Duverger (1905) emphasized the point of origin of the tumor. Pauliac (1911) noted a demarcation between the clinical picture of sarcoma and carcinoma; the former had the greater incidence before age 40, the latter, after 40. Soucy (1911) described a neurological form. Citelli (1911) reported an "endothelioma," retrotubal in origin, with early cervical gland metastases, and tinnitus and deafness treated erroneously for 4 to 5 months with tubal catheterizations. Rose and Lemaitre (1907) reported the syndrome of Avellis, consisting of paral-

ysis of the glossopharyngeal and vagus nerves, in a case of nasopharyngeal tumor. Trotter[3] reported "certain clinically obscure malignant tumours of the naso-pharyngeal wall." He noted the association of ipsilateral deafness, trigeminal neuralgia and palatal paralysis in these cases. Jacod (1914) described the invasion of the base of the skull along the Eustachian tubal cartilage by tumor. He noted also the invasion through the foramen lacerum and the cavernous sinus. His triad consisted of ipsilateral ophthalmoplegia, amaurosis, and trigeminal neuralgia. Vernet (1918) reported the jugular foramen complex of involvement of the glossopharyngeal, vagus, and accessory nerves in two cases of malignant nasopharyngeal tumors. Rouviere[5] (1932) reported the solitary involvement of the hypoglossal nerve by retropharyngeal nodes.

CASE MATERIAL.

This analysis covers 57 cases of primary malignant disease of the nasopharynx. The hospital service cases, 49 in number, covered the period from 1935 to 1960. The author's private cases numbered 11 (three of which were subsequently referred to the hospital and included in that group), covering a period from 1948 to 1960.

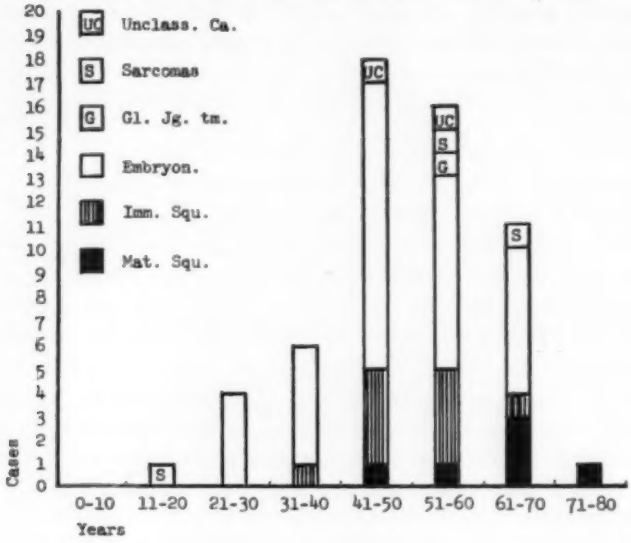
Age. The age ranged from 13 to 74 years. The average age for the total series was 49.6 years; for men, 51.2 years; for women, 44.7 years. The peak incidence was in the fifth decade. Thirty-four cases (60 per cent) were in the 41-60 year bracket.

The average age in the patients with embryonal cell carcinomas was 47.9 years; with immature squamous cell carcinomas, 48.7 years, and with mature squamous cell carcinomas, 62 years. (See Table I.)

In Digby's[6] series from Hong Kong the greatest age incidence occurred from 31-40 years; in Godtfredsen's[2] from Denmark and Sweden, 41-60 years. Digby had only one squamous cell carcinoma in 114 cases; Godtfredsen had 243 in 438 cases (55 per cent). In this series there were 16 squamous cell carcinomas in 57 cases (28 per cent).

The youngest patient in this series was 13 years of age; however, in the literature there are a number of reports of cases of malignant nasopharyngeal tumors occurring in children as young as two years.[10,11,14,15,18] Cancers of this region in children are about 1 per cent as frequent as in adults.[18] There have been several reports of cases in families. Pang[9] reported cases in a mother and son; McConnell,[16] in a brother

Table 1. Age Distribution with Reference to Histopathology.



and sister; Stinson[17] and Whiteleather[12] in two brothers, three years apart. Figi[13] reported the 10-year survival in the case of an 11-year-old boy.

Sex. There were 43 men and 14 women, a ratio of 3:1. In other reports the ratio of males to females varied from 2:1[21] to 4:1.[22]

Ethnology. In the total series there were 14 Chinese (25

per cent), 3 Negroes (5 per cent), and 40 Caucasians (70 per cent).

In the hospital series of 49 cases, there were 8 Chinese (16 per cent), 2 Negroes (4 per cent) and 39 Caucasians (80 per cent).

In the author's private series of 11 cases there were 8 Chinese patients (73 per cent), 1 Negro (9 per cent), and 2 Caucasians (18 per cent). The incidence in the Chinese patients was 1:33, in the others, 1:1200. Thus the incidence in the Chinese was 36 times greater.

It has been known for at least 40 years that nasopharyngeal cancer has a high incidence among the Chinese people.[6] Thus far, no satisfactory explanation for this racial predilection has been offered. Stout[23a] reported that 14 per cent of his cases were in Chinese, although the Chinese constituted only 0.3 per cent of the admissions to Presbyterian Hospital, New York. Martin and Quan[24] found no cases in American-born Chinese. They reported 37 Chinese in 358 cases (10 per cent). One of our Chinese patients was American-born. Pang[9] in Honolulu reported that in a series of 34 cases, 16 of his 27 Chinese patients (60 per cent) were American-born. Digby, Fook and Che[6] found that 18 per cent of all malignancies in the Hong Kong University Hospital were in the nasopharynx. Most of their cases were in Chinese. Bonne[25] found that cervical gland cancers ranked fourth among the Chinese in Batavia, but were absent from the reports of Tokyo. Dunlap[26] reported 16 cases in Chinese patients, none in Europeans, although 60 per cent of all his patients were Europeans.

Daito, Sakamoto and Hara[27] reviewed 68 cases which appeared in the Japanese literature. They cited Yamashita who reported 29 cases from Formosa. Four cases occurred in 12,000 Japanese, as opposed to 25 in 7,000 Chinese. The incidence in the latter (1:280) was 10.7 times that of the former (1:3,000). Hara[28] in Los Angeles reported 33 patients of whom 5 were Chinese (15 per cent), 2 Japanese, 1 Filipino, and 1 Negro. Since the Chinese constituted 0.2 per cent of the city's population, the incidence was 75 times the normal.

Das, Taneja, Chaddah and Minocha[29] undertook a study of the disease in Punjab, India, to determine whether nasopharyngeal cancer had a high incidence in all Orientals. They reported an incidence of 1.8 per cent of all cancer in outpatients, and 2.3 per cent in in-patients. These figures were in line with the incidence reported from the Occidental countries. Mekie and Lawley[30] reported that the third commonest type of cancer in Singapore, namely 16 per cent, was in the nasopharynx. All of their patients except one were Chinese. Djojopranto and Marchetta[31] reported a high incidence of nasopharyngeal cancer in the Indonesian natives. Of the total 8 per cent were in Indonesians, 14 per cent in Chinese living there. Garcia[32] reported that nasopharyngeal cancer was common among the Filipinos, but did not give exact figures.

Incidence in General. Reports from other countries have appeared, namely Australia,[33] Belgium,[34] Canada,[35-37] Cuba,[38] Denmark,[2] England,[8,20,39-43,54] France,[1,44,45,87] Germany,[46-49,127] Malaya,[30] Philippines,[32] Poland,[50] Spain,[51] Sweden,[52] and Switzerland,[121] indicating that the disease is encountered throughout the world.

At the Head and Neck Clinic of the Memorial Hospital in New York, Martin[22] reported an incidence of 2 per cent of all cancers. Simmons and Ariel[53] reported an incidence of 0.7 per cent of cancers at the Veterans Administration Hospital in Hines, Illinois. McPhee and LaCroix[36] reported an incidence of 2.5 per cent from Vancouver. Ormerod[54] reported an incidence of 8 per cent in the Otolaryngological Clinics in England. Godtfredsen,[2] in an excellent comprehensive monograph, reported 454 cases from four Radiological Clinics in Denmark and Sweden where the incidence was 0.8 per cent of all malignant tumors. There was an annual rate of 0.005 per cent in the general population.

At The Mount Sinai Hospital there was an incidence of 49 cases in 219,414 admissions to all the ward services, a ratio of 1:8,776, or rate of 0.011 per cent.

HISTOPATHOLOGY.

In this field there is divergence of opinion to the point of

confusion; however, there are a few points of common agreement. The tumors are highly malignant, and most of them are undifferentiated. There is a wide spectrum of variation in the degree of anaplasia in different parts of the tumor, in different patients, and in different times in the course of the disease; further, the appearance of the tumor may vary from the primary site when it metastasizes to different tissues. The tumors have a great tendency to spread in the lymphatic channels and to involve the regional lymph nodes very early. In later stages the liver and other parenchymatous organs, the bones, and distant lymph nodes are invaded.

The normal lining of the nasopharynx consists of a ciliated pseudo-stratified columnar epithelium in the upper part, and a stratified squamous epithelium in the lower part. In adults the ciliated epithelium is to a great extent replaced by squamous epithelium. After adenoidectomy stratified squamous epithelium replaces the respiratory type of epithelium.[55]

In the submucosa are varying amounts of lymphoid tissue, serous and mucous glands, blood vessels and lymphatic channels, and branches of the pharyngeal plexus, which include ninth and tenth cranial nerves, together with fibres of the sympathetic system.[2]

A voluminous literature on the classification and histogenesis of tumors of the nasopharynx has appeared in the past 60 years. Trotter[3] used the following classification:

1. Carcinoma: squamous and columnar;
2. Sarcomas of lymphoid tissue: lymphosarcoma, myxosarcoma;
3. Sarcomas of periosteal tissues: fibroma and fibrosarcoma;
4. Sarcomas of the wall: round cell, spindle cell, alveolar, and endothelioma;
5. Teratoma (or mixed elements).

It is likely that his "endothelioma" was the tumor later called "lymphoepithelioma."

Duval and Lacassagne[56] noted that the squamous cell carcinomas could be grouped into the differentiated (keratinizing) and undifferentiated types. There are many gradations from the extremely anaplastic to the mature type with pearl formation. Krompecher[57] believed that certain of the tumors were basal cell carcinomas.

In 1921 there appeared simultaneously in Germany, by Schmincke,[49] and in France, by Regaud and Reverchon,[58] descriptions of a distinctive type of tumor composed of epithelial elements intimately admixed with lymphocytic cells which they named lymphoepithelioma. Normal lymphoepithelium had been described earlier by Jolly.[136]

In the original article by Schmincke[49] the tumor is described as a cellular, diffusely infiltrating growth whose uniqueness rests in the syncytial structure which is permeated by lymphocytes. The cells are large, with rounded or oval vesicular nuclei, showing nuclear atypism, numerous mitoses, and varying amounts of chromatin with one or two prominent nucleoli. They occur in anastomosing cords or trabeculae and in nests or islands. Occasionally they break away and in areas may resemble sarcoma. Schmincke stated that the epithelial nature of the tumor was evident from the cellular and nuclear structure, type of growth, and relation to the stroma. He believed that these tissues arose from the branchial clefts where there is embryologically a close relationship between epithelial and lymphocytic elements. In an epithelial tumor of this origin, lymphocytic infiltration is to be expected. He emphasized that these are embryonal carcinomas.

There is no essential difference between the Schmincke and Regaud tumors.[66] Although many authors seem to think that Regaud's tumor is syncytial and Schmincke's is not, Schmincke clearly stated this fact in his paper. Both authors[49,58] noted that the tumors were radiosensitive, and metastasized early to the cervical lymph nodes.

In 1927 Quick and Cutler[59] reported a study of cervical lymph nodes invaded by metastatic carcinoma from primary

intra-oral lesions. These tumor cells were unusually radiosensitive, differed from squamous cell carcinoma, and presented transitional epidermoid characters. They noted that these tumors had been reported as anaplastic or embryonal carcinomas, and had been confused with sarcomas. They described an alveolar arrangement of polygonal cells, thought to arise in the ducts of mucous glands, or from squamous cells, or embryonic rests. Histologically, the cells have large hyperchromatic nuclei with pleomorphism, and scanty cytoplasm. The cells occur in groups or columns. There is an absence of keratinization and intercellular bridges.

It is interesting that the description of this tumor closely resembles that of the lymphoepithelioma; yet, in the confusion which arose, the term transitional cell carcinoma took hold and was cloaked with various meanings.[130] Some interpreted it as a tumor of a "new transitional" epithelium; others, of an undifferentiated tumor in transition toward the differentiated squamous cell carcinoma[131]; others, that the tumor arose from the basal layer of either the columnar or squamous epithelium. It must be pointed out that transitional epithelium occurs normally as such in the urinary bladder. In that location it is radioresistant. The normal epithelium in the nasopharynx is either of the columnar or stratified type, and no transitional zone has been demonstrated; furthermore, to confuse the relatively benign basal cell carcinoma of the skin with a "basal cell carcinoma" of the mucous membrane which is highly malignant, compounds the error. In cases which were reported as transitional cell carcinomas elsewhere, review of the slides has shown that these tumors belong either to immature squamous cell carcinomas, or to the tumors of the Schmincke type. It has been noted above that there is no essential difference between the Schmincke and Regaud types. It would be better, therefore, to regard both as embryonal cell carcinoma, and include certain of the undifferentiated "transitional cell carcinomas" in that category. The term "transitional cell carcinoma" should be discontinued.[60]

Stout[23a] omitted "transitional cell carcinoma" from his clas-

sification. Ewing,[61-64] Cappell,[65,66] and Eggston and Wolff[67] have indicated that it is often impossible to distinguish between "transitional cell carcinoma" and lymphoepithelioma; in fact, many have doubted whether lymphoepithelioma should be considered an entity.[2,6,68,69]

Since the term lymphoepithelioma is based primarily on the close admixture with lymphocytes in the stroma, it should be noted that the tumor grows on or into lymphoid tissue, and that varying infiltration with lymphocytes is seen as well in the squamous cell carcinoma and the "transitional cell carcinoma"[55]; therefore, until more is known about the histogenesis of these tumors it would seem reasonable to drop the term lymphoepithelioma and call these tumors *embryonal cell carcinomas.*[60]

Digby, Fook and Che[6,71] inclined to the view that the carcinoma arises from the columnar epithelium of the upper part of the nasopharynx. They state, "One section showed origin of the primary growth as arising from columnar epithelium at the junction where normal stratified epithelium meets normal columnar epithelium." [illegible]te that they saw no "transitional zone." They stated fur[illegible]er that "the term 'lymphoepithelioma' should be applied only where secondary deposits in tissues other than lymph glands show lymphoid as well as epithelial structure. This condition we have not found."

In 1936 Salinger and Pearlman[72] submitted slides to three eminent pathologists: Jaffe, Saphir, and Cutler. They found many instances of disagreement and confusion between "transitional cell carcinoma" and lymphoepithelioma, on the one hand; and between anaplastic carcinoma and "transitional cell carcinoma," on the other. Frank, Lev and Blahd[73] graded the tumors on the basis of whether the cells have a tendency to mimic the normal metamorphosis of cell types in stratified squamous epithelium. They attempted to classify the tumors which do not belong to the squamous group.

In Scandinavia much study has been devoted to the problem of classification of these tumors. On the basis of mor-

phology and special staining techniques, especially silver impregnation, Ahlström[52] declared that the lymphoepitheliomas belong to the reticulum cell sarcoma group. Kreyberg,[74] however, recognized that some lymphoepitheliomas belong to the undifferentiated carcinomas and some to the reticulum cell sarcomas. There are many adherents to both sides on this point. Ringertz[75] emphasized the difficulty of distinguishing sufficiently between a carcinoma of low-grade differentiation and an undifferentiated reticulum cell sarcoma.[2,67]

In this paper embryonal cell carcinomas are considered of epithelial origin and are classified separately from the reticulum cell sarcomas.

The sarcomas, as a rule, are multicentric, and may be considered a systemic disease from the outset.[23a] These are malignant tumors derived from embryonal connective tissue, or mesoderm. They may be classified as lymphosarcoma of *1.* small round cell type (lymphocytic); *2.* large round cell type (reticulocytic); *3.* undifferentiated cells simulating epithelial cells. The sarcomas tend to be exophytic and slow growing. They frequently produce a large primary mass (or masses) before metastasis occurs. These tumors respond to radiation for a time but recur and metastasize.[67,70] Other sarcomas which may occur in the nasopharynx are the following: Angiosarcoma, fibrosarcoma, angiofibrosarcoma, chondrosarcoma, rhabdomyosarcoma, and plasmocytoma.[129,132] Other epithelial tumors which may occur are adenocarcinomas arising from glands or their ducts in the mucosa.[55]

Saphir[55] lists angioendothelioma and malignant melanoma as very rare. Chordomas and meningiomas may invade the nasopharynx as secondary growths. Plasmocytoma was reported by Schall and Cordray,[76] and by Waltner.[77] Rhabdomyosarcoma was reported by St. John and Zung-Pah Woo[7] in a four-year-old boy, and Holborow and White[8] in a four-year-old girl. Both had a rapidly fatal course.

In this series, the available slides were reviewed by the

author.* The tumors were classified in three main groups: squamous cell carcinoma, embryonal cell carcinoma, and sarcoma (see Table II). The squamous cell carcinomas were divided into mature and immature types (see Figs. 1-3). There were various gradations of differentiation from immature squamous carcinomas, which had features of embryonal cell carcinoma, to mature carcinomas with keratinization and pearl formation. Similarly the embryonal cell carcinomas varied from typical Schmincke tumors (see Figs. 4-5) to those resembling reticulum cell sarcomas. Of the three cases of sarcoma, one (Case 31) was a lymphosarcoma which later

TABLE II.

Distribution of Histopathology.

Histopathology	Cases	Per Cent
Mature Squamous Cell Carcinoma	6	11%
Immature Squamous Cell Carcinoma	10	18%
Embryonal Cell Carcinoma	35	61%
Unclassified Carcinoma	2	3%
Sarcomas: Angiofibrosarcoma Lymphosarcoma Reticulum Cell Sarcoma	3	5%
Glomus jugulare tumor	1	2%
	57	100%

metastasized to an inguinal node and appeared as a reticulum cell sarcoma (see Fig. 6); one (Case 46) filled the nasopharynx, then involved the lateral walls of the pharynx and later extended to the hypopharynx; and one (Case 55) was an angiofibrosarcoma in a 13-year-old Negro girl, with a fulminating course characterized by massive tumor, polyp hanging down to the epiglottis, fever, and death in seven weeks from date of admission (see Fig. 7). The possibility that this was a malignant change in a juvenile fibroma was considered; however, Gisselsson, Lindgren and Stenram[78] found no authenticated cases in females; there was no antecedent history to indicate a pre-existing juvenile fibroma;

*The author expresses his appreciation to Dr. S. Otani and Dr. W. Mautner of the Department of Pathology at The Mount Sinai Hospital for their valuable assistance.

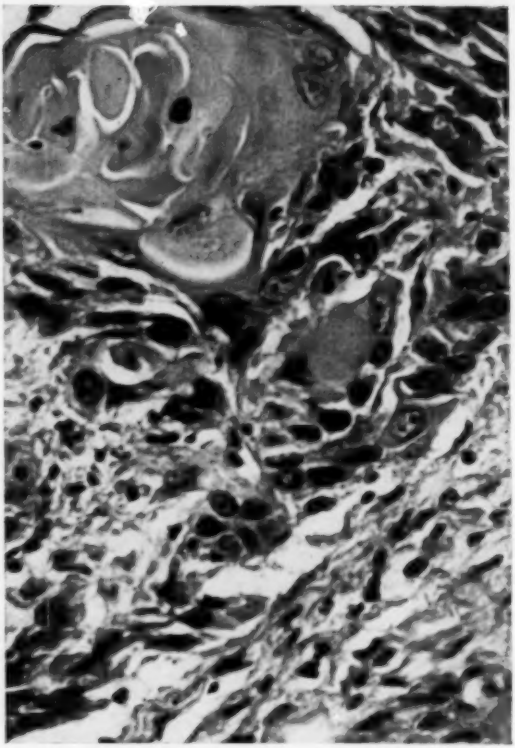


Fig. 1. (Case 38)—Photomicrograph of mature squamous cell carcinoma, showing keratinization with pearl formation. (x 400)

the tumor hardly bled when it was removed for biopsy; and the course was that of a highly malignant neoplasm.

In addition, one patient (Case 43) with a glomus jugulare tumor was included, because it appeared from careful review, that the tumor arose in the antero-lateral wall of the nasopharynx (nasal surface of the soft palate) and proceeded to invade the lateral wall of the nasopharynx and nose, as well as the petrous pyramid, and later metastasized to the thoracic vertebra. This case was reported by Rosenwasser[79] as an

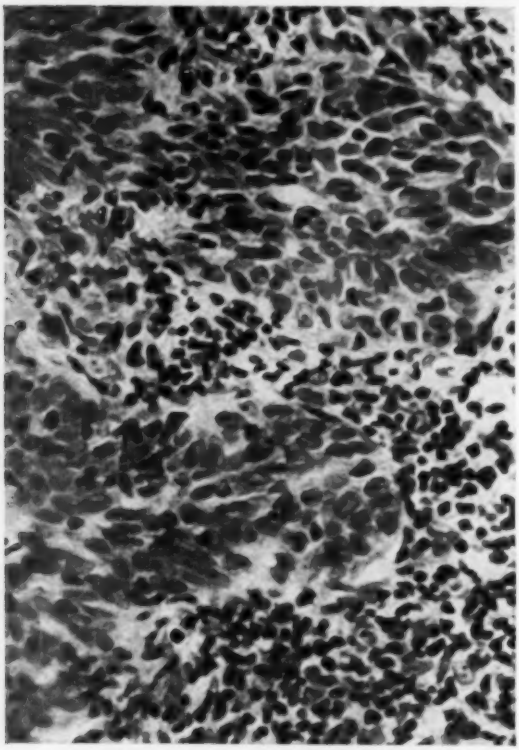


Fig. 2. (Case 5)—Photomicrograph of immature squamous cell carcinoma. Previous diagnosis elsewhere was transitional cell carcinoma. (x 400)

example of a metastasis from glomus jugulare tumor. These tumors may arise at a distance from the jugular bulb,[80] and in fact do arise anywhere in association with the pharyngeal plexus.

Finally, there were two cases which were carcinomas, but could not be further classified, because the cells in the original slide showed a squeezing effect. (See Table II.)

TOPOGRAPHIC ANATOMY.

The nasopharynx, situated just beneath the base of the

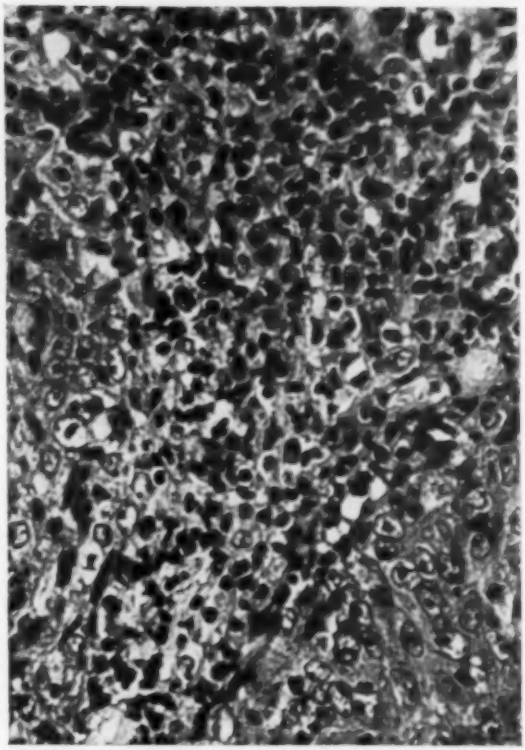


Fig. 3. (Case 26)—Photomicrograph of immature squamous cell carcinoma with features of embryonal cell carcinoma in this area of tumor. See edge of tumor in lower right hand corner. Note lymphocytic infiltration of stroma. (x 400)

skull, is in intimate relation to the body of the sphenoid bone above, the basilar process of the occipital bone behind, and proceeding from the midline laterally, the sphenopetrosal fissure, the apex of the petrous pyramid, the foramen lacerum, the foramen ovale and foramen spinosum, and the root of the greater wing of the sphenoid. Curving forward, the attachment of the pharyngobasilar fascia is in relation to the medial lip of the scaphoid fossa, and the medial lamina of the pterygoid process.

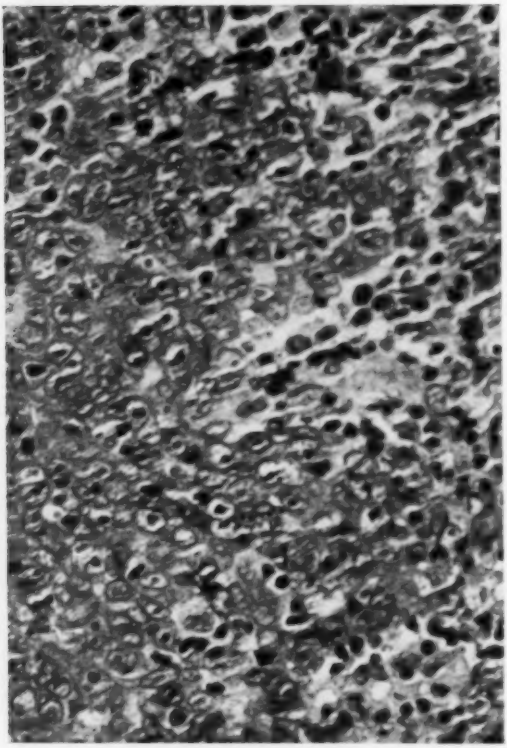


Fig. 4. (Case 29)—Photomicrograph showing typical embryonal cells with vesicular nuclei and prominent nucleoli. Note admixture with lymphocytes. (x 400)

Superiorly, extension of a nasopharyngeal tumor may involve the sella turcica, dorsum sellae, and the posterior clinoid process; laterally, the apex of the petrous pyramid and the root of the pterygoid process.

Anteriorly, the nasopharynx opens to the nasal cavity through the choanae separated by the posterior border of the nasal septum; thus, the space and walls of the nasal cavity, the turbinates, the ethmoids, and the maxillary antrum may be invaded. Through the lamina cribrosa invasion may proceed to the anterior cranial fossa. Through the ptery-

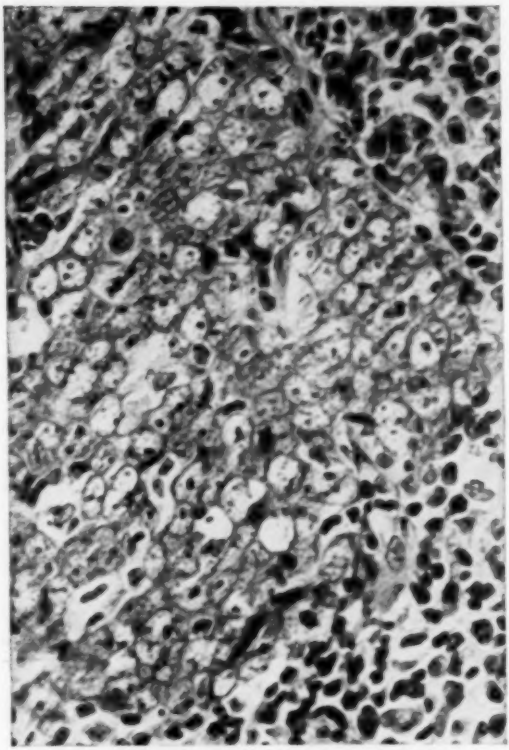


Fig. 5. (Case 57)—Photomicrograph showing closely packed tumor cells, syncytial in character, with frequent mitoses. Note intense infiltration with lymphocytes and plasma cells. (x 400)

gopalatine fossa, which is traversed by the second division of the trigeminal nerve, invasion may proceed through the superior orbital fissure into the orbit above, and the infratemporal fossa laterally. Through the latter, the pterygoid muscles and the parotid gland may be reached.

Posteriorly, the retropharyngeal space, the prevertebral fascia, and the muscles are passed, after which the anterior arch of the atlas is reached. Through this, the spinal canal and the posterior cranial fossa may be invaded.

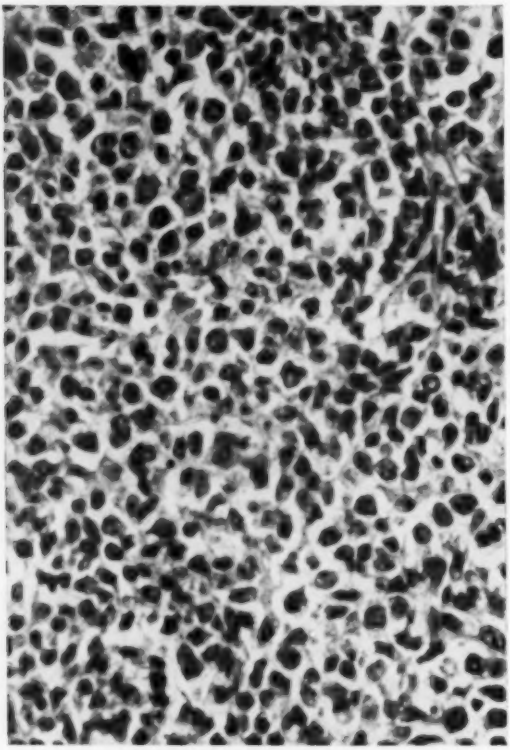


Fig. 6. (Case 31)—Photomicrograph of reticulum cell sarcoma in metastatic inguinal node. Biopsy of nasopharynx showed lymphosarcoma. (x 400)

Inferiorly, the soft or hard palate may be displaced or infiltrated with involvement of the palatine arches, the palatine tonsils, the base of the tongue and hypopharynx.

The nasopharynx is an air-containing space communicating anteriorly with the nose, laterally with the middle ears, and inferiorly with the oropharynx. In the vault in embryonic life are the remains of the notochord, and the origin of Rathke's pouch. In childhood, the adenoids and masses of lymphoid tissue are present. Although these structures re-

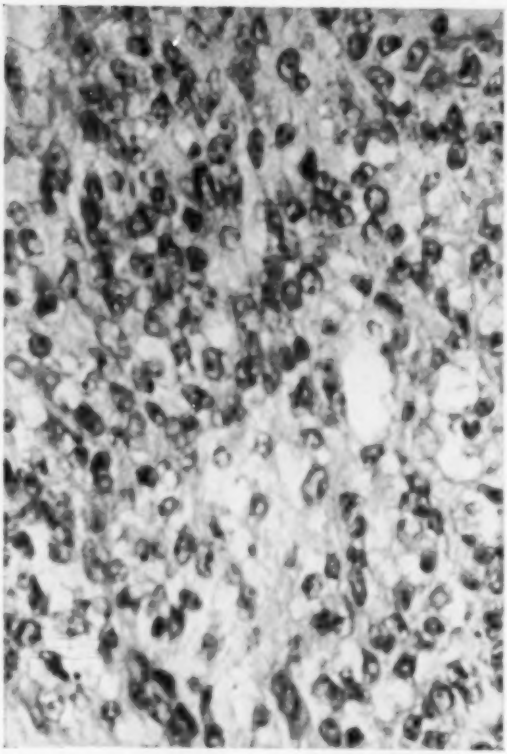


Fig. 7. (Case 55)—Photomicrograph of angiofibrosarcoma. Note vascular channels. (x 400)

gress after puberty, varying amounts of lymphoid tissue persist. Occasionally the pharyngeal bursa forms a pouch which may be involved in Tornwaldt's disease.

On the side wall is the lateral recess, or fossa of Rosenmüller. This contains a varying amount of lymphoid tissue termed the tubal tonsil. Just anterior to it is the torus tubarius and orifice of the Eustachian tube.

The floor of the nasopharynx is formed in part by the upper aspect of the soft palate, and opens to the oropharynx.

Lymphatics. Special mention must be made of the lymphatic system in its relation to the nasopharynx. The entire region is traversed by lymphatic vessels which communicate freely across the midline; thus, bilateral involvement of the cervical glands is the rule, although one side often is affected first, and the involvement is usually not symmetrical. The lymph glands in the retropharyngeal space are first to become involved.

The deep cervical nodes lie in chains along the internal jugular vein. In addition, there are the superficial nodes, the subdigastric, inframandibular, submaxillary, spinal accessory, and supraclavicular nodes.[2,5,81]

SYMPTOMATOLOGY.

As will be inferred from the topographic anatomy, the symptoms of this disease are kaleidoscopic. They can be best considered by separating them according to cervical, nasal, otic, ophthalmic, neural, and general symptoms.

The shape of the nasopharynx has been compared to that of a prompter's booth.[2] The analogy can be pursued further. The prompter, though located in front of the stage, is hidden from the audience, as the tumor in the nasopharynx is hidden from the physician. The prompter indicates the signals for the dramatic action; similarly, the tumor can evoke a variety of clinical pictures.

1. Cervical Symptoms.

Enlargement of lymph glands in the neck may be the first symptom. Frequently the upper deep cervical node just beneath the posterior border of the sternomastoid[81a] muscle at the level of the angle of the jaw is the first to be noticed by the patient. The swelling may be accompanied by tenderness or pain, but usually it is painless. A mass may be present for three or four months before the patient seeks medical advice. Often, the patient will delay until a mass appears on the opposite side of the neck.

In this series, 16 patients (28 per cent) complained of

swelling in the neck on admission. The average duration was 4.7 months.

2. Nasal Symptoms.

Early in the disease there may be none in this category. There may be intermittent stuffiness, usually unilateral, or a slight mucoid or blood-stained discharge. Late in the disease, the discharge may become fetid as a result of tumor necrosis. Anosmia was noted in two cases. Involvement of the paranasal sinuses occurs late, but may be the condition which causes the patient to seek medical care for the first time. Epistaxis usually occurs late in the disease, and at that time may be severe enough to require hospitalization. In general the occurrence of unilateral persistent nasal obstruction in a middle-aged patient should arouse suspicion of a neoplasm. In this series 25 patients (44 per cent) complained of nasal symptoms when first seen.

3. Otic Symptoms.

Symptoms of tubal occlusion may be the first to bring the patient for examination. Usually unilateral, these range from a slight feeling of fullness, clicking sensations, or stuffiness, to pain and discharge. Consequent to the tubal occlusion, conductive type of hearing impairment ensues. Tinnitus may be the first symptom. In the case of glomus jugulare tumor it was present for three years before the tumor became evident by bulging of the soft palate (Case 43).

In this series, 23 patients (40 per cent) had symptoms of tubal occlusion, five had tinnitus, three had otalgia, three complained of hearing impairment, and one had vertigo.

4. Ophthalmic Symptoms.

Most of the early symptoms referable to the eyes are properly considered under the neurological heading. The most common is diplopia (eight cases). Next, in order, are ptosis (three cases), and proptosis (two cases). In the late cases, loss of vision (four cases) may occur as a result of invasion of the orbit, or involvement of the optic tracts after the tumor has eroded the sella turcica. Symptoms referable to

the eye occurred initially in 11 cases (20 per cent), and in the fully developed picture in 15 cases (26 per cent).

5. Neural Symptoms.

The widest range of symptoms was found in this category. The most common was headache. This appeared initially as the only symptom in 14 cases (25 per cent). The next most frequent were disturbances of the trigeminal nerve: incidence eight patients (14 per cent). These ranged from mild paresthesias and hypesthesias, to severe paroxysms of pain.

The loss of the sense of smell, the symptoms due to impairment of the auditory nerve and vestibular nerve, and the symptoms due to involvement of the optic, oculomotor, trochlear and abducens nerves were noted above. In addition, facial paralysis was the chief complaint in one patient (Case 9). Difficulty in swallowing, regurgitation of food into the nose, and nasal quality of speech were noted in 14 cases. Cough and hoarseness were noted in five cases. Pain and stiffness in the neck were noted in three cases. Difficulty in speech was noted in two cases. Total incidence of neurological symptoms: 26 patients (45 per cent).

6. General Symptoms.

It is noteworthy that in this disease there is general well-being until the advanced stage is reached.

Loss of weight does not occur until there is interference with swallowing or metastasis to the liver and bones. It was noted on admission in 12 cases (21 per cent).

Fever occurred in the one case of angiofibrosarcoma. (See Table III.)

In the literature the duration of symptoms before diagnosis was as follows: Furstenberg[82]: 15 months; New[83]: 14 months; Hauser and Brownell[84]: 12 months; Kleinfeld[85]: eight months; Thompson and Grimes[86]: eight months; and Pang[9]: six months. Note that there has been a steady shortening of the duration of symptoms prior to diagnosis in more recent years. Godtfredsen[2] reported the range of duration

of the first symptom as two weeks to 5.6 years. In half the cases, it was six months or less.

In the author's total series the average duration of symptoms was 8.8 months, ranging from two weeks to three years; however, the reduction in the average duration of symptoms

TABLE III.

Frequency of Initial Symptoms.

Region	Symptom	Incidence	Patients	Per Cent
1. Cervical	Enlargement of cervical glands	16	16	28%
2. Nasal	Obstruction	15		
	Discharge	12		
	Bleeding	10		
	Anosmia	2	25	44%
3. Otic	Tubal occlusion	23		
	Tinnitus	5		
	Conductive hearing impairment	3		
	Otalgia	3		
	Vertigo	1	23	40%
4. Ophthalmic	Diplopia	8		
	Ptosis	3		
	Proptosis	2	11	20%
5. Neural	Headache	14		
	Pain, paresthesias numbness of face	8		
	Facial paralysis	1		
	Difficulty in swallowing, nasal regurgitation, and nasal speech	14		
	Cough, hoarseness	5		
	Pain, stiffness of neck	3		
	Difficulty in speech	2	26	45%
6. General	Loss of weight		12	21%
	Fever		1	2%

became strikingly apparent when the series was divided into three succeeding periods: 1935-1944: 12.6 months; 1945-1954: 6.8 months; and 1955-1960: 6.4 months.

PHYSICAL FINDINGS.

Most of the patients with nasopharyngeal cancer give no outward indication of the disease. As has been stated before, general well-being is the rule, except in the advanced stages of disease when cachexia has developed.

1. The Primary Lesion.

On casual inspection of the pharynx there may be no indication of the danger that lurks behind the palatine curtain. Bulging of the soft palate was seen in only five cases. On indirect mirror examination of the nasopharynx one may see only a fullness of the posterior wall, or narrowing of the fossa of Rosenmüller, with intact mucosa; or, there may be a slightly raised granular lesion with intact or ulcerated mucosa on the posterior wall, the vault, the lateral wall, or the fossa of Rosenmüller. The torus tubarius may be compressed or covered with dusky lymphoid tissue. There may be hypertrophy of the postero-lateral bands of lymphoid tissue extending down into the oropharynx. This was seen in a patient with lymphosarcoma (Case 46).

Occasionally the lesion is exophytic in type. The mucosa is granular and friable. In one patient (Case 55) a polyp arising in the nasopharynx hung down into the hypopharynx and touched the edge of the epiglottis. This was an angiofibrosarcoma.

There may be a slight fullness of one or both tonsils.[125] In the advanced cases, the tumor may occupy the entire nasopharynx, and the point of origin be obscured. There were five such cases.

Geist and Portmann[21] described the tumors as ulcerated, lobular and exophytic. The ulcerated tumors were usually in the vault, and were differentiated squamous cell carcinomas. The lobulated tumors on the lateral wall or recess were transitional cell carcinomas or lymphoepitheliomas. The exophytic tumors were on the posterior wall, usually sarcomas.

Baclesse[87] described the tumors in 128 cases according to location as postero-superior: 60; lateral: 48; anterior: 3; and non-classifiable: 17. Bach, Lederer and Palevsky[88] reported a case in which tumor cells were implanted on an ulcerated area of the upper surface of the soft palate.

In the present series, the location of the tumor bore no relation to the histopathology, except in the instances of sarcomas mentioned above.

2. Cervical Adenopathy.

Enlarged cervical glands were palpable on admission in 34 patients (60 per cent). In 18 patients, the adenopathy was bilateral. The incidence in relation to histopathology is shown in Table IV.

TABLE IV.

Cervical Adenopathy with Reference to Histopathology.

Histopathology	Cases	Involved	Per Cent
Squamous Cell, mature	6	2	33%
Squamous Cell, immature	10	7	70%
Embryonal Cell	35	23	66%
Unclassified Ca.	2	1	50%
Sarcomas	3	1	33%
Glom. jug. tum.	1	0	0%
Total	57	34	60%

The incidence of cervical adenopathy on admission, in the literature, is shown in the following table:

Godtfredsen[2]	32%
Hara[28]	33%
Mattick and Marchetta[122]	33%
Legler[48]	40%
New[83]	42%
Fox[89]	42%
Hickey[14]	42%
Scanlon *et al.*[10]	47%
Martin and Blady[91]	50%
Wang[92]	50%
Digby[6]	64%
Geist and Portmann[21]	65%
Pang[9]	65%
Graham and Meyer[93]	70%
Kleinfeld[85]	75%
Lederman[41d]	75%
Kramer[94]	76%
Simmons and Ariel[53]	83%

3. Nasal Findings.

In general, the appearance of the nasal mucosa and turbinates gave no indication of the disease in the nasopharynx. In only two cases neoplastic tissue was seen posteriorly near the floor and lateral wall of the nasal cavity. The maxillary antrum was invaded by tumor in two cases; in 11 cases there was evidence of secondary infection. The sphenoidal sinuses were invaded by tumor in two cases; and were clouded on radiography in 12 cases. There was radiological evidence of disease in the ethmoids in seven cases. The frontal sinus was involved in only one instance. Incidence of nasal findings was 18 patients (32 per cent).

4. Otic Findings.

Although 23 patients had symptoms of tubal occlusion on admission, only 13 patients had a conductive hearing loss. There was a perceptive element in six of the 13 patients. There were absent caloric responses in one patient. The tympanic membrane lacked lustre or was thickened in five cases. There was unilateral otitis media in three cases. Incidence of otic findings was 23 patients (40 per cent).

On radiography there was evidence of destruction involving the apex of the petrous pyramid in five cases (9 per cent).

Druss[95] reported a case in which squamous cell carcinoma had invaded the petrous pyramid, after having first caused suppurative mastoiditis by tubal occlusion. He found evidence of carcinomatous invasion in the perineural lymphatics. Rarely, tumor tissue grows through the middle ear and appears in the external auditory canal.[96]

5. Ophthalmic Findings.

The abducens nerve was involved in 14 (25 per cent), the oculomotor nerve, in 11 (20 per cent), and the trochlear nerve, in six patients (11 per cent).

There were unilateral proptosis in three (5 per cent), optic atrophy in three, and papilledema in one patient. Incidence of ophthalmic findings was 25 per cent. (See Figs. 8-11.)

In Schlivek's[97] series of 38 cases there was involvement of the ophthalmic division of the trigeminal in 12, Horner's syndrome in ten, abducens in eight, ophthalmoplegia in four, proptosis in two, papilledema in one, optic atrophy in one, and orbital mass in one.

6. Neural Findings.

The great variety of findings in this category lends a unique fascination to this disease.

Fig. 8. (Case 54)—Photograph showing unilateral proptosis and ptosis. Complete ophthalmoplegia was present. (Embryonal cell carcinoma.)

The trigeminal nerve was most frequently involved. This may be explained by the close anatomical relationship of the fossa of Rosenmüller to the point of exit of the trigeminal nerve, and by the manifold opportunities for contact provided by the three sensory divisions of the nerve and its motor branch in their respective extracranial courses. Incidence: 19 patients (33 per cent). The motor branch was involved in three cases (5 per cent).

The acoustic, abducens, oculomotor, trochlear, and optic nerves were considered in the preceding sections.

The glossopharyngeal nerve was next in order of frequency of involvement. Incidence: 14 cases (25 per cent).

The vagus was involved in five cases (9 per cent), and the accessory in four cases (7 per cent).

The facial nerve was involved as the presenting symptom in one case. Involvement was found in seven cases on admission, or 12 per cent. The intracranial portion of the facial nerve is usually involved only very late in the disease and

Fig. 9. (Case 54)—Patient after seven weeks of Cobalt ^{60} teletherapy. Note remission of proptosis and recovery of function of levator palpebrae superioris. Patient was able to move eye in all directions.

may be spared because of its higher position in the posterior fossa.[98] It may also be involved during its course in the temporal bone. In the latter cases there is often associated involvement of the acoustic nerve.

The auditory branch of the acoustic nerve was involved in six patients (11 per cent). The vestibular branch was involved in two cases (3 per cent).

The hypoglossal nerve was involved in eight cases (14 per cent), usually in association with the glossopharyngeal and vagus in the jugular foramen syndrome.

Isolated involvement of the XIIth nerve was seen once (Case 4). This was due to pressure from involved retropharyngeal glands, and cleared up after radiotherapy.

Pressure on the vagus may result in hoarseness and cough due to vocal cord paralysis. Incidence: five cases (9 per cent).

Isolated involvement of the accessory nerve was reported

Fig. 10. (Case 56)—Photograph showing bilateral ptosis, and left external strabismus, due to complete oculomotor paralysis. Patient has metastasis to liver and bones, weight loss. (Immature squamous cell carcinoma.)

by Digby[6] who showed photographs of patients with atrophy of the sternomastoid and trapezius muscles. Incidence: four cases (7 per cent).

The glossopharyngeal, vagus, accessory and hypoglossal nerves, as well as the sympathetic trunk, may be involved extracranially as a group in the region of the jugular foramen either by pressure from nodes or invasion by tumor. They

may also be involved intracranially by extension of the tumor through the anterior arch of the atlas into the cervical canal and posterior cranial fossa.[2] Horner's syndrome due to involvement of the sympathetic trunk was noted in eight cases (14 per cent).

The olfactory nerve was involved in only two cases (3 per cent).

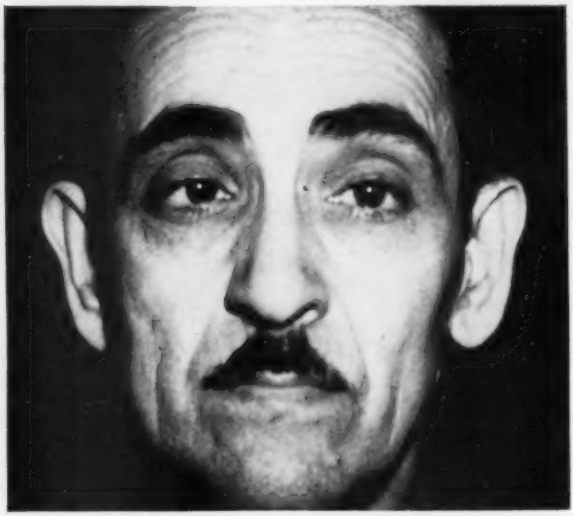


Fig. 11. (Case 57)—Photograph showing slight ptosis and right internal strabismus, due to partial paralysis of oculomotor and right abducens nerves. Patient has enlarged liver, weight loss. (Embryonal cell carcinoma.)

One patient (Case 17) had involvement of all 12 cranial nerves. Universal involvement was reported by Flynn[99] in one case, and Simmons and Ariel[53] in two cases.

Needles[98] reported 35 cases of nasopharyngeal tumors from the neurological aspect. He stressed the "infelicitous tendency to invade the base of the skull while remaining silent at the original site in the nasopharynx." He noted further that

although the sella turcica may be destroyed, and the pituitary body be surrounded by tumor, signs of dyspituitarism did not appear. This fact was also noted by Bach, Lederer and Palevsky.[88]

In Needles' series,[98] 45 per cent had involvement of cranial nerves. He found cranial nerve involvement in the following order of descending frequency: Vth, VIth, IIIrd, and IVth. He noted that although the tumor remained extradural in most cases, Ballenger[100] found an exception in which the tumor invaded the temporal lobe, posterior part of the frontal lobe, pons, optic tract and chiasm.

Godtfredsen[2] reported neurological signs in 38 per cent. Of these, 71 per cent involved VIth, 59 per cent Vth, 54 per cent IIIrd and IVth, and 39 per cent jugular foramen syndromes.

Woltman[101] analyzed the neurological findings in 25 of 79 cases of nasopharyngeal tumors reported by New,[19] and found involvement of the Vth in 17, VIth in 18, IXth and Xth in nine, IInd in five, IIIrd in four, IVth in four, XIth in three and XIIth in five.

Brock[23c] reported cranial nerve involvement in 50 per cent of the cases. He noted that the trigeminal involvement in tumors of the nasopharynx differed from paroxysmal trigeminal neuralgia in that the latter revealed no objective sensory changes and no muscle involvement.

Lenz[102] in a report on 91 cases, noted that the cranial nerves in the carotid sheath closest to the retropharyngeal nodes were compressed earliest: the vagus and hypoglossal in 16, cervical sympathetic in 10, glossopharyngeal in 10, and spinal accessory in 1 instance. By contrast, nerves compressed intracranially are more frequently involved beginning with the lowest in anatomical position; *i.e.*, trigeminal 19, abducens 17, oculomotor eight, trochlear five, facial four, and optic two. He noted that intracranial involvement was more frequent in epitheliomas (squamous cell carcinomas) than in the lymphoepitheliomas (embryonal cell carcinomas).

Flatman[41c] reported Snelling's [41b] 78 cases of nasopharyngeal tumor from the neurological aspect. He found involvement in 30 patients. The order of frequency was almost identical with that in the present series. He made radiographic studies of a section of the head in which the cranial nerves had been dissected out and replaced with wires of similar gage. He noted that the greater superficial petrosal nerve is closer to the nasopharynx above the fossa of Rosenmüller than any of the other nerves. Lederman[41d] noted that

TABLE V.

Cranial Nerve Involvement with Reference to Histopathology.

Cases	Histopathol.	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	H.*	Involv.	Per Cent
6	Squ. Cell, mat.	1		3		5	4	1	2	4	1			2	5	83%
10	Squ. Cell, imm.	1	2	2	2	3	2	2	3	2	1	1	2	1	4	40%
35	Embryonal		2	6	4	10	7	3		6	2	2	5	5	15	43%
2	Unclass. Ca.						1	1	1	1	1	1	1		1	50%
3	Sarcomas					1				1					1	33%
1	Gl. jug. tum.															0%
57		2	4	11	6	19	14	7	6	14	5	4	8	8	26	45%

*Horner's syndrome.

the loss of the corneal reflex is sometimes the first sign of intracranial invasion.

Molony[103] reported neurological involvement in 15.8 per cent; Scanlon, Devine and Woolner,[10] in 28 per cent; and Pang[9] in 47 per cent.

Involvement of the cranial nerves and sympathetic trunk (Horner's syndrome) in relation to the histopathology is shown in Tables V and Va.

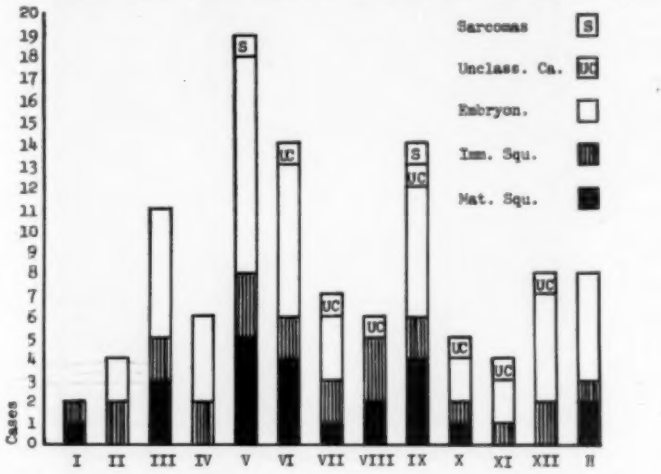
It will be noted that the order of involvement of the cranial nerves in decreasing frequency is what one would expect from the discussion in the initial symptomatology, namely: Vth sensory, VIth, IXth, IIIrd, XIIth, Horner's syndrome, VIIth, IVth, VIIIth, Xth, XIth, Vth motor, Ist. Total incidence: 26 cases (45 per cent).

The chart shows a greater involvement of cranial nerves in the mature squamous cell carcinomas (83 per cent) than in the embryonal cell carcinomas (43 per cent).

7. Radiographic Findings.

The radiographic findings of the base of the skull range from a slight enlargement of a foramen to evidence of destruction of the body or wings of the sphenoid, the clivus, the posterior clinoids, or sella turcica. Incidence: 14 cases (25 per cent). There may be destruction of the basiocciput. Occasionally widening of the petrosphenoidal suture is noted.

Table 5a. Cranial Nerve Involvement with Reference to Histopathology.



The apex of the petrous pyramid may be involved (five cases, 9 per cent). (See Figs. 12, 14, 15.)

The mass in the nasopharynx may change the contour of the air column. There may be widening of the retropharyngeal space. (See Fig. 13.)

Clouding of the sinuses occurred frequently (22 cases, 39 per cent). Metastasis to the maxillary antrum was found twice, Case 56. (See Fig. 16.)

The orbit revealed destruction of the medial wall in one case.

Fig. 12. (Case 44)—Radiograph (mento-vertical view) showing destruction of basisphenoid, including clivus and root of greater sphenoid wing, and petrous apex, as well as sphenoid sinus on the right side. (Mature squamous cell carcinoma.)

Destruction of the base of the skull on radiography occurred with greater frequency in the squamous cell carcinomas (six of 16 cases, 38 per cent), than in the embryonal cell carcinomas (six of 35 cases, 17 per cent).

8. Distant Metastases.

Involvement of other than regional lymph nodes occurred in four cases (7 per cent). Metastasis to the liver was found in five instances (9 per cent). Metastasis to the bones, par-

ticularly the vertebrae, occurred in seven cases (12 per cent). One patient had a tumor in the stomach which responded to radiotherapy for a time. The parotid gland was involved in two cases. Fein[119] reported a lymphoepithelioma in the parotid gland.

Distant metastases occurred with greater frequency in the embryonal cell carcinomas (16 of 35 cases, 46 per cent), than

Fig. 13. (Case 44)—Radiograph (lateral view) showing displacement of air column by large tumor in nasopharynx, and destruction of basisphenoid. (Mature squamous cell carcinoma.)

in the squamous cell carcinomas (three of 16 cases, 19 per cent).

Baclesse[87] reported distant metastases of 32 per cent in the lymphoepitheliomas (corresponding to embryonal cell carcinoma), and 19 per cent in the epitheliomas (squamous cell carcinomas).

Fig. 14. (Case 47)—Radiograph (mento-vertical view) showing shadow of tumor with destruction of base and clivus of sphenoid, and foramen ovale on the right, with extension to right sphenoid sinus. (Embryonal cell carcinoma.)

DIFFERENTIAL DIAGNOSIS.

Given an adult with a lesion in the nasopharynx, cancer must be presumed present until proved otherwise.[53,104]

In the presence of cervical adenopathy, or any nasal, otic, ophthalmic, or neural symptoms, a biopsy should be taken of any suspicious lesion, or even fullness, in the nasopharynx.[105] Where a constellation of symptoms exists, biopsy is warranted even when nothing abnormal is apparent to the

Fig. 15. (Case 48)—Radiograph (base view) showing radiolucent area of destruction of sphenoid and basiocciput. (Immature squamous cell carcinoma.)

naked eye; indeed, a second or third biopsy is sometimes required to prove the diagnosis. In this series a positive diagnosis was obtained by biopsy in three cases in which all that could be seen was a slight fullness of the posterior wall near the fossa of Rosenmüller. In two cases, biopsy was repeated when the first report was negative.

If examination with the mirror is difficult, the pharynx should be anesthetized. A catheter may be passed into the nasal cavity and brought out through the mouth to be used

Fig. 16. (Case 56)—Radiograph showing tumor mass in right maxillary antrum.

as a palate retractor for better visualization by indirect examination.[39] The electric nasopharyngoscope should be used, although its field of vision is limited. The Yankauer nasopharyngeal speculum is a useful instrument for examination and biopsy.

The biopsy should be deep enough to obtain submucosal tissue. A small sharp punch forceps should be used so that

the specimen will not be squeezed. Squeezing renders histopathological examination difficult, if not impossible. Biopsy under local anesthesia is an office procedure. General anesthesia is required only in children.

Morrison, Hopp and Wu[106,107] advocated the Papanicolaou-Trout smear technique for early diagnosis of lesions in the nasopharynx. They recognized that the technique does not replace biopsy. The author believes that there is no need to use the technique. In the diagnosis of nasopharyngeal tumors precise histopathological information and localization of the lesion are required. Often the lesion is deeper than the mucosa, and even a superficial biopsy would be inadequate. No reliance can be placed on a negative report of a smear.

Lenz[102] advocated radiographs in the anteroposterior, mentovertical and lateral views of the skull. Baclesse[87] used lipiodol instilled into the nasal cavity to delineate the nasopharynx. Arnold and Baylin[108] outlined methods of establishing a radiographic diagnosis, using the lateral, frontooccipital, mento-vertical, base, and Stenver's views.

Radiographs can be used for confirmation of a clinical diagnosis and for evaluation of progress of the disease, but the chief reliance must be placed on a careful clinical and histopathological examination.

Primary malignant tumors in the nasopharynx are to be distinguished from the following: *1.* Juvenile fibroma, a benign tumor, which occurs in adolescent males and produces an exophytic lesion which bleeds profusely; *2.* secondary growths involving the nasopharynx include chordomas, craniopharyngiomas, meningiomas, and teratomas.[55]

Inflammatory lesions such as tuberculosis frequently cause cervical adenopathy. Pulmonary lesions are almost always associated.

The lymphomas are also to be considered.[90] Lymph node biopsy should confirm the diagnosis. The report of a malignant tumor on excision of a cervical node where the primary

lesion is undiagnosed makes a naso-pharyngeal biopsy mandatory.

Mistakes in Diagnosis. New[83] reported 185 operations and procedures which had been performed erroneously on 194 patients (95 per cent) prior to referral to the Mayo Clinic. Kleinfeld,[85] Furstenberg,[82] Hauser and Brownell,[84] Godtfredsen,[2] and Gollom[35] have reported erroneous diagnoses and mistaken treatments in 25-33 per cent of the cases. Grotts[11] reported the case of a two-year-old girl who had been subjected to incision for a "retropharyngeal abscess" where "granulation tissue" was found on two occasions prior to referral for proper diagnosis and biopsy.

In this series only five cases (8.7 per cent) had been operated upon erroneously prior to referral. Alcohol injections were given for trigeminal neuralgia, and a submucous resection, an ethmoidectomy, an adenoidectomy, and a nasal polypectomy were performed.

TREATMENT.

Prior to 1900 surgery and electrocoagulation were used with completely unsuccessful results. In the past 60 years various combinations of X-irradiation and radium emanation have been employed.[12,13,23e,102,110,116,118,134,135]

It is not considered within the scope of this report to describe the details of radiation therapy; however, at the present time, in this institution, the plan of radiation therapy employed for cancer confined to the nasopharynx is the administration of 5000 to 6000 r in five to six weeks to the entire nasopharynx. With orthovoltage in the 200 to 400 k.v. range, four portals are required: two pre-auricular and two antral. With Cobalt 60 teletherapy or supervoltage, the tumor dose can be administered through the pre-auricular fields alone. When the cervical glands, orbit, paranasal sinuses, base of the skull, or other sites are involved, additional therapy is directed to those areas.[109]

During the administration of radiation therapy, supportive measures are added. These include high caloric and high

vitamin diet, dental hygiene, and symptomatic therapy as needed. The hematologic status is checked periodically. The treatment is conducted on an ambulatory basis in most cases.

Lenz[102] uses a tumor dose of 4500 to 5000 r in the cases of lymphosarcoma and lymphoepithelioma, and 6000 to 7000 r in epithelioma (squamous cell carcinomas). He notes that supplemental radium applications did not affect the course of the disease. Scanlon, Devine and Woolner[10] agreed with this observation. Sooy[111] reported the experimental use of electrodesiccation followed by Cobalt 60 teletherapy. Smedal and Watson[112] reported the use of 2,000,000 volt irradiation in 39 patients, using 6000 r to the tumor over a period of seven weeks.

Daito, Sakamoto and Hara[27] in 1952 and later Hara[28] in 1954, advocated the surgical extirpation through the transpalatal approach for adenocarcinoma, the angiosarcomas and fibrosarcomas, as well as the well localized lymphomas, followed by electrodesiccation and deep X-irradiation. The results in these cases have yielded a 13 per cent survival. Flatman[41c] expressed dissatisfaction with palatal fenestration because patients have developed intracranial extension without visible disease in the nasopharynx. Hara[28] preferred X-irradiation as the treatment of choice for squamous cell carcinoma, lymphoepithelioma and lymphosarcoma. Pang[9,113] employed palatal fenestration followed by application of radium (500 mg. hrs.) to the lesion at the time of surgery. His results yielded a 12 per cent survival. He stated that neck dissection was indicated only when the primary lesion is definitely controlled by irradiation. Farrior[113] adhered to this view, and preferred neck dissection in squamous cell carcinoma, but was dubious in the lymphoepitheliomas. Hilger[114] expressed disappointment with the results of neck dissection. He stated that recurrences require further irradiation, rather than surgery.

It would appear that primary reliance for treatment in malignant disease of the nasopharynx should be based on deep irradiation, either by conventional orthovoltage or supervoltage teletherapy.

In this series of 57 patients, a complete course of X-irradiation was administered to 45 patients (a supplementary application of radium was given to one patient), Cobalt 60 teletherapy was administered to two patients. Five patients were untreated. In five other patients treatment was interrupted because of extremely advanced disease. Chemotherapy was used in three refractory cases with some amelioration of symptoms and delay of the final outcome.

Results of Treatment: Survival. Nineteen (40 per cent) of the 47 treated patients are alive. Fifteen (32 per cent) of these patients are free from disease. Thirty-eight patients were treated from 1935-1955. Of these, 11 patients (23 per cent) have been observed for periods ranging from six to 25 years (average 12½ years) and have revealed no sign of recurrence in the nasopharynx or elsewhere since the end of treatment. One patient, treated in 1952, was free from disease for eight years, but developed recurrent disease in the cervical nodes. The enlargement disappeared after a second course of X-irradiation in May 1960.

Of the seven survivors who were treated within the past five years, one is free from disease for four years, two for three years, and one for one year. The three remaining patients have persistent disease.

The absolute five-year survival rate is 29 per cent (11 of 38 patients). Three of these patients were lost to follow-up; thus the determinate five-year survival rate is 31 per cent (11 of 35 remaining treated patients).

All but one of the 12 patients who have survived longer than five years, had embryonal cell carcinoma; the exception had an unclassified carcinoma. Of the seven survivors who were admitted within the past five years, five had embryonal cell carcinoma: three are free from disease, and two have persistent disease. Of the remaining two who had immature squamous cell carcinoma, one is well for three years, and one has distant metastases. None of the patients with mature squamous cell carcinoma, lymphosarcoma, reticulum cell sarcoma, angiofibrosarcoma, or glomus jugulare tumor survived.

It is difficult and unrealistic to compare the survival rates in the literature because of the lack of uniform criteria as to types of tumors included, length of observation period, classification of histopathology, and differences in methods of calculating the results. Frequently the published rates are the determinate rather than the absolute figures. The author

TABLE VIa.

Results of Treatment: Survival with Reference to Histopathology.
a. Patients admitted between 1935-1955.

Histopath.	Cases	Radiotherapy No	Radiotherapy Yes	n.e.d. 5 yr.	Survival Recurr. disease	Rate
			3	0		0%
Mat. Squ. Cell	6	3		0		0%
			5	0		0%
Immat. Squ.	6	1		0		0%
			25	10	1	40%
Embryonal	29	4				
Unclass. Ca.	2		2	1		50%
Sarcomas	2		2	0		0%
Glom. jug.	1		1	0		0%
Totals	46	8	38	11	1	29% (Abs.)
			-3*			
			35			31% (Det.)

*Lost to Follow up.

TABLE VIb.

b. Patients admitted between 1955-1960.

Histopath.	Cases	Survival n.e.d.	dis.
Imm. Squ. Cell	4	1	1
Embryonal	6	3	2
Sarcoma	1	0	0
	11	4	3

has reviewed 33 reports in which the five-year survival rates range from 0 per cent in the period before 1940 to 25 per cent in recent years. It would appear that factors operating to increase the survival rates have been *1.* earlier diagnosis; *2.* presence or absence of metastases, especially bone involvement; *3.* improved radiation techniques.

RECURRENCES.

It was not unusual for cervical lymph nodes to become palpable during treatment or shortly after it was completed. This occurred in 12 cases within five months. In eight additional cases recurrences took place within 22 months. The average was 9.3 months. Five patients had multiple recurrences. One patient with an embryonal cell carcinoma (Case 4) had eight separate recurrences over a period of 15 years. He was treated with X-irradiation for each episode and led a useful existence up to within two months of his death. One should not assume that if the disease does not recur within an arbitrary period of two, three, or five years, that the patient is cured. One patient (Case 39) who was well for eight years developed cervical adenopathy, which responded well to another course of therapy. Babcock[23b] reported a case with recurrence after nine and one-half years.

The tumor recurred in the nasopharynx in only three patients.

MORTALITY.

Of the total 57 patients admitted between 1935 and 1960, there were 32 deaths. Three of these were due to other causes: Laennec's cirrhosis, aortic stenosis, and postoperative cardiac failure. Six patients were lost to follow-up. The net mortality due to tumor was 29 of 51 patients (56 per cent).

The terminal event was recorded in only seven instances: nasal hemorrhage, three; respiratory obstruction, two; aspiration of food, one; coma, one.

There were 11 autopsies performed. There were metastases to the liver in three, intracranial invasion in three, vertebral invasion in five.

With reference to histopathology, 16 deaths occurred in the embryonal cell carcinomas (46 per cent of 35 cases), six in mature squamous cell carcinomas (100 per cent of six cases), five in immature squamous cell carcinomas (50 per cent of ten cases), three in sarcomas (100 per cent of three

cases), one in glomus jugulare tumor (100 per cent), and one in unclassified carcinoma (50 per cent). (See Table VII.)

DURATION OF DISEASE.

For the 32 patients who died, the duration of disease was calculated as an average of 24.5 months. The range was from two to 160 months. This is not an accurate figure, because the estimate of duration of symptoms was in many

TABLE VII.

Mortality and Duration of Disease with Reference to Histopathology.

Histopathology	Cases	Mortality	Rate	Duration of Disease (Months)
Squamous Cell, mature	6	6	100%	10
Squamous Cell, immature	10	5	50%	16
Embryonal Cell Ca.	35	16	46%	42
Unclassified Ca.	2	1	50%	23
Sarcomas	3	3	100%	10
Glomus jugulare tumor	1	1	100%	72
	57	32	56%	24.5

TABLE VIII.

Mortality and Duration of Disease with Reference to Periods of Time.

Periods	Cases	Mortality	Rate	Duration of Disease (Months)
1935-1944	15	10	66%	32
1945-1954	30	17	56%	22
1955-1960	12	5	41%	17
	57	32	56%	24.5

cases obviously too brief. There is no way of determining how long the disease was present before some symptom was noticed by the patient.

In the course of this study, it was observed that in the early period most of the patients were admitted in the late stages of disease. With the passage of time there has been a steady shortening of the delay in diagnosis and an improvement in the condition of the patients on referral. The series was divided into three periods: 1935-1944, 1945-1954 and

1955-1960. The mortality and duration of disease were then analyzed with reference to these periods. It will be seen that the mortality rate has been reduced from 66 per cent for the first period, to 56 per cent for the second, and 41 per cent for the third; however, it is too early to evaluate the results in the third period. (See Table VIII.)

STAGES OF DISEASE.

Geist and Portmann[21] established a useful classification:

Stage I —Tumor confined to the nasopharynx.

Stage II —Palpable nodes in addition.

Stage III—Local invasion of orbit, sinuses, or base of skull in addition.

In this series, with one exception, the patients who were in Stages I and II when treatment was begun were the only ones to survive for more than five years.

COMMENT.

It is evident that it is essential for all physicians to be aware of the eventuality of cancer of the nasopharynx when presented with symptoms arising from surrounding structures. The medical profession cannot evade the responsibility for a delay of several months in making the proper diagnosis. The improved prognosis provided by radiation therapy should serve to encourage the physician to consider this disease more readily.

It would be advisable to examine adenoids removed at operation for histopathology when there is any suspicion of abnormality.

This author believes that the incidence of cancer of the nasopharynx is greater than is generally considered. Many cases are not diagnosed. It is recommended that a sphenoid block including the nasopharynx be removed in all post-mortem examinations.

SUMMARY.

Analysis of 57 cases of malignant tumors of the nasopharynx has revealed that the histopathology is a significant factor in the clinical picture, results of treatment, survival, mortality, and duration of disease.

Embryonal cell carcinoma (commonly referred to in the literature as lymphoepithelioma) has a far better prognosis than squamous cell carcinoma. Experience with sarcoma in this study revealed a gloomy prognosis.

Early diagnosis plays an important role. The only patients who survived more than five years were those in whom the disease had not progressed beyond metastasis to the regional lymph nodes when treatment was begun. No patients with cranial nerve involvement were "cured" of disease.

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CORRECTION.

We have been requested to make the following correction in the paper, "Foreign Body Complications," by Dr. Paul G. Bunker, in the August 1961 issue:

On page 907, the third paragraph, eighth line, the word "dysphagia" should read "odynophagia".

On page 908, the first paragraph, last line, the word "emphysema" should read "empyema".

THE PARANASAL SINUSES.
SUMMARY OF LISTINGS IN THE INDEX MEDICUS FOR 1960.

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Part I.

PREFACE.

All of the listings in the Index Medicus for 1960 have been examined. Only those which seemed to be more important have been abstracted. The remainder have been briefly mentioned for the purpose of keeping the bibliography complete.

ANATOMY.

Wende[1] attempted to determine whether a unilateral overdevelopment of the frontal sinus could be related to cranial hypoplasia by studying a series of 1,165 pneumoencephalograms. He found five instances of a unilateral frontal sinus enlargement in conjunction with a dilatation of the ventricle, three times on the same side and twice on the contralateral side.

The exceedingly small number of associated intracranial pathologies in connection with unilateral enlargement of the frontal sinus demonstrated in this series, leads to the conclusion that the latter, without evidence of other cranial bone dystrophies, cannot be ascribed to cranial damage in early childhood.

Susse[2] seems to think that asymmetry of the frontal sinuses may have some pathologic significance. He finds that 60 per cent of such cases have an associated headache. In seven out of eight total aplasia cases, headache was a constant symptom. On the contrary 88 per cent of patients with normally developed frontals had no headache; furthermore, the author

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was struck by the presence of a facial hemangioma in five patients with asymmetrical frontals. Other cranial abnormalities have been noted in these cases, which leads him to conclude that asymmetry of the frontals as shown in the X-rays may be an index of the general development of the skull and its contents.

PHYSIOLOGY—PATHOLOGY.

Beidler[3] reports the results of investigations of the mechanism of taste and olfactory reception in animals through electrophysical experiments. These demonstrate the different manner in which stimuli to these special senses are received and evaluated. Whereas the olfactory receptors are well protected, as are the visual and auditory receptors, the gustatory sensory end-organs are more exposed and are, therefore, protected by a different mechanism, namely, the ability to regenerate taste bulbs following trauma.

Taste cells which are innervated by the chorda tympani and the glosso-pharyngeal reproduce each other through mitotic division. There are not more than a few thousand nerve fibers supplying these cells as compared to millions of olfactory fibers. The experiments of Beidler showed that while some fibers respond chiefly to one taste quality, all of the fibers are capable of responding to a lesser degree to other qualities.

The olfactory sense functions quite differently. The receptors are bipolar neurons and not differentiated epithelial cells, and their dendritic processes number into the millions. These receptors respond to concentration of odors a million times more dilute than is the case with the gustatory sense. Discrimination of odors is presumed to depend upon the molecular structure of the particular particle inhaled and its reaction to the host of receptors.

The experiments were conducted on rats by means of electrical stimulation of the terminal nerve fibers and the responses recorded through an oscilloscope and a Sanborn recorder. It was shown that the trigeminal nerve participates

in odor detection at various levels although to a different degree than the olfactory nerve.

De Lorenzo[4] examined the olfactory mucosa and papillae foliato of the rabbit under electron microscopy and found some marked differences in their receptor mechanism. Since no definite structural variation could be demonstrated in the olfactory receptors, discrimination of odors can be attributed only to the varying reactions of the receptors to molecules of varying structure. The fine structure of the receptor cells, their supporting cells and the arrangement of the ciliary processes, are all beautifully seen through the electron microscope.

Examination of the taste buds by this method reveals receptor cells in various stages of development, thus demonstrating the rapid turnover as new cells replace the old. This suggests that new nerve fibers are constantly regenerating and that specificity of function is determined by the axon to cells' contiguity at any particular time.

Nikolaevskaya[5] conducted a number of experiments on dogs to determine the effect on respiration of various stimuli applied to the mucosa of the frontal sinus. A trephine opening was made into the sinus and a duraluminum tube hermetically sealed into the fistula. After all inflammatory symptoms had subsided, the following stimuli were applied through the tube: tactile, by means of a cotton wrapped wire; thermal, by means of water at different temperatures; chemical, by solutions of penicillin, hydrochloric acid and caustic soda; air under pressure of varying degrees and oxygen. In the great majority of the experiments it was noted by the kymographic tracings from the pneumograph, that these stimuli caused an increase in the amplitude of respiration and reduction in the rate.

It was interesting to observe that oxygen proved to be a less potent stimulus than air. The author concludes that the sinuses take part in the regulation of respiration.

Fabricant[6] lists the recent contributions to the subject of

nasal physiology, most of which appeared in my abstracts for 1959 (*Arch. Otolaryngol.*, 73:196-243, Feb., 1961).

Breuninger[7] tested the reaction of the nasal mucosa to hypertonic and hypotonic solutions of salt and dextrose. He found that the hypertonic solutions evoked a response from the mucosa in the form of increased secretion, the degree depending on the concentration of the solution. Since no damage was inflicted on the ciliated epithelium the conclusion is that the increased flow of mucus was due to osmotic pressure. Hypotonic solutions caused no reaction. The clinical significance of these findings is that hypertonic solutions which increase the osmotic pressure, without the addition of other active substances, result in ciliary damage as shown by Proetz.

Cranmer[8] describes cytomegalic inclusion disease as a generalized salivary gland virus infection which occurs more frequently in children and still-born infants. It is characterized by "owl-eyed" giant cells with nuclear and cytoplasmic inclusions.

The case which he reports was in a 56-year-old female who complained of sneezing, burning sensation in the nose and thin yellowish discharge. Examination revealed swollen nasal mucosa studded with small granular lesions of a papillary nature. This hyperplastic tissue was removed with difficulty due to hemorrhage. Histologic examination showed edematous soft membrane with small polypoid nodules arising from the surface. Large cells were seen in which the prominent nucleus was surrounded by a clear halo. "In more advanced lesions the epithelial cells appear distended by large inclusion bodies which are sharply outlined, round, and show moderate variation in size." In cases of this kind, which appear to be localized in the respiratory passages, laboratory studies should be made of nasal and salivary secretions and the urinary sediment for the diagnostic cell. The case cited by the author revealed numerous epithelial cells in the urine but none with inclusion bodies; granular casts and a few red blood cells also were present. This raised a suspicion that early renal cytomegalic disease was developing.

Van Lier[9] tested the sneeze reflex and the mucosal reaction to an irritant in three classes of patients, namely, 45 controls, 75 patients with non-atopic vasomotor rhinitis and 45 with specific vasomotor rhinitis (pollen or house dust). The tests were made by blowing a mixture of pepper with amylum oryza in two concentrations, one to 20 and one to one. Based on the reactions observed, the author determined that the sneeze reflex threshold was much lower in the atopic vasomotor cases than in the non-atopic cases, or in the normal. He concludes that the autonomous nervous system may play an important part in some patients with both types of vasomotor rhinitis.

McLaurin, Shipman and Kirkley[10] describe a new apparatus for the measurement of nasal capacity which they have employed for the purpose of determining the effectiveness of various nasal decongestants orally ingested. The technique employed is a modification of the Seebohm-Hamilton method whereby the mouthpiece is replaced by a Boothly-Lovelace-Bulbulian nasal oxygen mask to which a pressure transducer is attached. Fall-in pressure within the mask is transmitted to the pressure transducer, its "output fed to the recorder, and the number obtained in millivolts is readily converted to centimeters of water pressure."

Both the objective or rhinometric and the subjective results are tabulated from tests on 31 patients with four of the principally used vasoconstrictors.

Calearo and Lazzaroni[11] examined specimens of the olfactory mucosa from humans as well as from a number of mammals (Equus caballus, Bos taurus and Canis familiaris), staining them with hematoxylin-eosin, azar, alcian blue 8GN and toluidine blue. Several of the slides are reproduced in the article. They were able to demonstrate acid mucopolysaccharides in the layer above the epithelium, the olfactory epithelium and in Bowman's glands.

Differences in the chromotropia were found between various species, being present in a pH of 2.2 in canines as compared to pH of 4 in herbivorous animals. The histochemical analysis

of these elements serves to explain the mechanism of odor perception whereby the reaction of the sensory cells to the stimulus of the molecules in the air-borne particles is effected.

Ferrari and Zini[12] studied the effects of aniline products on the nasal mucosa of rabbits by injecting a 1 per cent sol. of 25 per cent pure aniline in olive oil subcutaneously and by subjecting them to exposure to inhalations of vapor impregnated with aniline. The results of their investigation showed marked degenerative lesions of the olfactory bulb and neurosensorial cells of the olfactory mucosa following the injections and irritative and degenerative lesions of the mucosa including the olfactory elements following inhalations but with less general effect on the entire neural mechanism. These investigations were undertaken to demonstrate the occupational hazards of workmen exposed to coal product derivatives in the manufacture of dyes and various pharmaceutical products.

Majer[13] employing silver stains of Bielchonsky-Gros and Jabonero, demonstrates granulomas consisting of large ramified anastomosing prolongation cells of various sizes and shapes in the nasal polypi of allergic individuals. These and other silver staining granules as well as perivascular fibrillary differentiated neural formations, correspond to Jabonero's vegetative terminal formation.

Animal experiments after repeated anaphylactic shock show an increase of silver positive prolongation cells and an injury to the vegetative terminal formation. Treatment with Cortisone results in the disappearance of the granuloma knots as well as a decrease in the number of eosinophiles.

Acharyya, Hazratt and Chakbrabarti[14] sought to evaluate the adrenocortical function in 14 cases of nasal allergy by taking a differential blood count before and after the injection of .3 cc. of epinephrine solution. Normally the injection causes neutrophilia, lymphopenia or eosinopenia. Reduction of eosinophil count by more than 50 per cent indicates normal adrenocortical function. In the series of patients tested, nine out of the 14 showed depressed function, that is, the decrease

in eosinophils was less than 50 per cent. The mechanism of the response is discussed, particularly with reference to the role of the glucocorticoids. They state that "treatment by the antihistaminics or glucocorticoids is a vexed problem even when there is normal adrenocortical response after epinephrin injection in allergic rhinitis."

DIAGNOSIS.

Bryan and Bryan[15] in a beautifully illustrated article with colored microphotographs, demonstrate the value of cytologic examination of nasal smears. A swab carried along the floor of the nose will yield not only the epithelial cells but the goblet cells as well, which, when properly stained, will contribute materially to the diagnosis. They show the findings in allergy, the common cold, bacterial infections and occasionally a malignancy. An interesting finding is the giant cells which can be recovered in measles and are considered pathognomonic. The detailed description of the various cells found in the conditions mentioned are given at some length. This contribution should act as a stimulus for all otolaryngologists to pursue this valuable diagnostic procedure.

Cytologic examination of antrum punctate[16] was carried out in 68 cases: 42 cases of cancer were diagnosed, mixed tumor seven, malignancy without histologic determination, gigantoma one, maxillary cyst five and inflammatory process two. These were all done for diagnosis of suspected tumors.

Buraggi[17] presents one of the best articles on the interpretation of laminagraphs of the maxillary sinus that has appeared in many years. The pictures are taken in three planes: sagittal, occipito-fronto-nasal, lateral and axial submento-vertex. These are all illustrated with accompanying explanatory diagrams. Only certain areas of the sinus can be accurately defined as to the integrity of the walls and pathology in the interior—these correspond to the medial area seen in the sagittal projection (median strata), the medial portion of the sinus seen in the lateral projection (level II), and the superior region (first level), and the posterior area examined in the axial projection.

The pictures and diagrams show clearly how shadows derived from the mandible, the alveolus, the petrous bone, etc., are seen in the pictures and how they can be identified and distinguished from pathology in the antrum. This article is very instructive.

Freienstein[18] describes a simple procedure for taking sinus pictures in infancy and early childhood. The baby is placed in a "Babyfix" apparatus made of plastic material. The arms are drawn up on each side of the head and bound together. The feet are also bound. A pillow under the neck prevents the child from dipping the chin. Shifting of the head is prevented by the fitting of the cage in which it rests. The central ray passes through the maxilla between the tip of the nose and the mouth—distance 100 cm., the tube being tilted caudally about 27°.

Wilson[19] analyzes the roentgenographic procedures employed in a series of 435 facial bone fractures and describes the varieties of projections required for different types of injuries. The article is well illustrated with drawings showing the mechanics of displacement, the X-ray findings, and the procedures employed for reduction. He gives the details of the different projections that were used.

Marques and Bellossi[20] demonstrate the value of a horizontal planagraph taken in the Hirtz projection (vertex on the plate), which visualizes the posterior part of the maxillary sinus, posterior ethmoids, sphenoid, and the pterygo-maxillary region. When the projection is correct, the shadow of the mandible is out of the way. This picture shows the borders of the antrum in its posterior region in its relationship to the pterygo-maxillary fossa and is valuable in the determination of the extent of involvement in cases of malignancy. One can see the curved line of the posterior border of the antrum and its junction with the pterygoid plate. This knowledge is very important when the therapy is outlined.

When one is familiar with this projection and has learned to identify the various lines as shown in the illustration, there is much that can be learned.

Krahl[21] calls attention to the spinal fluid changes which may be of some value in determining the advance of malignancies of the epipharynx and sinuses toward the base of the skull and spinal column. If the spinal fluid protein content is less than 50 mg. per cent, it may be assumed that the lesion has progressed only to the dura. With higher values, it may be assumed that the growth has penetrated the dural barrier.

Gerlings[22] finds transillumination of the sinuses of little value in diagnosis and often misleading. He cites several cases such as an abnormally small antrum on one side, a cyst, fluid and thickening of the mucosa as examples of pathology that presents simply a cloudy sinus and that the diagnosis can be made only by careful X-ray studies.

COMPLICATIONS: INTRACRANIAL—ORBITAL.

Arndt and Rudschies[23] report a case in which a frontal lobe abscess was removed 18 years after an apparently successful resection of an osteomyelitic process of the frontal bone. The patient suffered no ill effects during this long interval except for one brief episode of pain and swelling over the eye. When the abscess was exposed and removed, its walls were found to be very thick, as was the dura overlying it. This would indicate that it had been present for a long period of time. The diagnosis was made from the ocular symptoms plus the findings on arteriography.

Bonnal, Girard, Bremond and Fagalde[24] had a case in which a purulent sphenoiditis caused erosion of the superior and lateral walls with invasion into the extradural space, forming an abscess and compressing the optic nerve, causing blindness. The X-ray pictures showed the extent of the bony involvement which was at first attributed to a carcinoma or a chondroma. The true pathology was disclosed when a frontal craniotomy was performed. The authors' comment points to the need for more careful nasal examination since suspicion of the sinus origin would make the surgery less risky if performed endonasally.

King[25] reports a case of fulminant frontal sinusitis which

ran a brief stormy course ending in death before surgical measures could be adopted. Autopsy revealed a large subperiosteal abscess, erosion of both plates of the frontal sinus, a large subdural abscess over both frontal lobes and thrombophlebitis of the superior sagittal sinus. Cultures yielded staphylococci—coagulase positive, strain 80/81. It was apparent that the infection had been transmitted from the mother who had a suppurating hidradenitis of the axilla which yielded the same organism as was found in the boy's case.

Gsell[26] found that there are 30 different etiological possibilities in serous meningitis of which only six are quite common in central Europe. Investigations in Switzerland were successful in differentiating about 80 per cent of these cases. To date, the epidemiological and serologic studies have been very helpful, but there is need for more knowledge about all the known organisms. The author presents a full list of the different types of infective agents he isolated in these cases and classifies them according to the laboratory procedures employed.

Vivell[27] lists the following viruses as having been identified in connection with upper respiratory infections:

Myxovirus influenza, Types A and B.

Unclassified as yet, Type D causing pneumonia and abacterial meningitis.

HE type 1E upper respiratory infections with temperature.

CA (Croup assoc.) causing laryngo-tracheobronchitis.

Myxovirusparotitis (mump virus) causing parotitis, pancreatitis, orchitis and meningoencephalitis.

Also Myxovirus multiforme (New Castle disease), pneumoencephalitis.

Myxovirus pertigalli (Gefluegelpest).

Fliss[28] reports several cases of orbital involvement from pathology in the frontal sinuses. These include, mucocele, osteoma, carcinoma and caseous sinusitis. He suggests col-

laboration between ophthalmologist, rhinologist and roentgenologist in such cases.

Leeson[29] reports a case of pansinusitis in a girl of ten which developed into an orbital abscess, going on to an ophthalmoplegia and accompanied by Jacksonian seizures. Recovery followed prompt drainage of the antrum via an intranasal antrostomy, external ethmoid exenteration of the ethmoids and opening the frontal sinus with exposure of the dura. A penicillin sensitive Staph. aureus was recovered.

It is interesting to note in Feng's report[30] of a series of 57 cases of retrobulbar optic neuritis that although an ethmoiditis was found in only two cases, a total of 40 normal ethmoids was opened resulting in a cure of nine, marked improvement in nine and slight improvement in eight. This would tend to substantiate the rationale of ethmoidectomy formerly practiced with enthusiasm and later discarded.

In the present series the author admits that the etiology was unknown in 40 per cent of the cases and attributed to facial infection in 46 per cent.

Baldwin[31] reports a case of exophthalmos in a male age 38 which was thought to be due to a tumor or extensive polyposis, and when the orbit was explored through a fronto-ethmoid incision a large subperiosteal abscess with numerous polypi was found. The process had eroded the orbital plate of the maxilla, lacrimal bone, floor of the frontal sinus, lamina papyracea, interfrontal septum, nasal bone, anterior wall of the sphenoid and part of the nasal septum. Staph. aureus was isolated. Initial improvement was later followed by recurrence of the symptoms, and consequently a Caldwell Luc and transantral ethmoidectomy were done with exenteration of diseased mucosa and polyps. Complete restoration of ocular function was achieved.

Privara[32] reports seven cases of thrombosis of the cavernous sinus, six of which terminated fatally. They were well advanced when first seen. From the point of view of etiology the author reviewed a series of 19 cases and found that furunculosis of the nose or face was the most common cause

(nine cases). Six were due to intranasal infection; one to dental, and one to an ear infection. This report would seem to indicate that there still are areas in the world where antibiotics are not employed to the extent to which we are accustomed.

Poccianti's[33] case of osteomyelitis of the superior maxilla in an infant of 40 days ran a chronic course for several months before it was cured. The infective organism was the Staph. aureus which was found to be sensitive to novobiocin and erythrocyn. There were two draining fistulae: one near the root of the nose; the other, in the gingival recess. The author states that X-ray pictures cannot be relied upon for diagnosis in the progress of the case, but he finds that the sedimentation determination is of much greater value.

Yarington[34] presents a case of cavernous sinus thrombosis in a child of ten, giving a history only of a recent trauma. The symptoms and findings were characteristic, and the child recovered after intensive antibiotic therapy supplemented by trypsin. There were no after effects, and the child was found to be normal when seen four years later.

THE SINUSES IN CHILDREN.

Cavanaugh[35] claims that in the course of 100 years only 152 cases of osteomyelitis of the superior maxilla have been reported in the literature, yet she has encountered 24 cases during the past 17 years; 14 of which occurred during the first three months of life. The symptoms seem to follow a pattern, with swelling of the lids, cheeks, alveolus, purulent nasal discharge and fistulae in various areas of the face and jaw appearing in nearly all of the cases. Information as to the source of the infection was indefinite and could be directly attributed to puerperal sepsis, breast abscess in the mother in only three cases. As to bacterial invaders, the Staphylococcus aureus was the most common, having been found in 16 cases.

The author shows pictures of several typical cases.

The treatment followed was quite simple. Systemic antibiotic therapy, antrum puncture with indwelling polyethylene tube for continued drainage. The author decries the incision of the alveolus as endangering the tooth buds. Nothing is said about the management of sequestrums.

Hubble[36] discusses the factors responsible for recurring colds in children and the development of the chronic catarrhal state, namely, environmental, allergic and local and congenital. These are analyzed at some length. The author considers the disease as developing in three stages: the initial stage of recurring colds with variable catarrh and nasal obstruction; the stage of established lymphoid hypertrophy, and, finally, the stage of complications, sinusitis, otitis media and lower respiratory disease. In the initial stage, if there is a history of recurring complications, it is wise to administer penicillin or other antibiotics as a prophylactic against resurgence of latent bacterial infection. Nose drops preferred are those made up with Ringer's or Tyrode's solution.

Regarding the second stage of lymphatic involvement the author is inclined to be conservative but feels that surgery is definitely indicated when the middle ear is frequently involved.

If the sinuses are affected nothing need be done locally unless a purulent infection is demonstrated. Because of the frequent association between the latter and bronchiectasis, the author feels that direct therapy to the sinuses is indicated, even to the point of surgical drainage.

Biesalski and Marquardt[37] tested the reaction in the nasal mucosa of infants by means of thermo-electric measurements during the employment of various types of decongestive agents. They were thus enabled to supplement their clinical observations through the temperature readings. They found that of all the vasoconstrictors that were used, the best results were obtained with ortrivine (2-4′-ter-butyl-2, 6′ [dimethylphenylmethyl]-imidazoline). This agent gave satisfactory degrees of decongestion with less rebound than any of the others.

MALIGNANT TUMORS.

The literature on tumors of the sinuses has been voluminous. There still exists a division of opinion on the question of preoperative irradiation as against postoperative. Hilger[38] feels that preliminary irradiation will block the lateral pharyngeal node which is not resected in the resection of the neck. He advises super voltage irradiation primarily followed in six weeks by opening the antrum, inspection of the field, taking of biopsies for frozen section and subsequent treatment of residual carcinoma by radical maxillectomy if needed. Gabka and Singer[39] also suggest preliminary irradiation followed by surgery. They point out a factor that influences the prognosis, namely, that a mucosal carcinoma which frequently originates in the alveolus can be detected earlier than an antrum carcinoma; they point also to a fallacy in interpreting statistics. To obtain the whole truth one must include all of the cases that were not operated. One can naturally show better results by analyzing only those cases that were considered operable in the first place.

Most of the other reports favor postoperative irradiation. Barbossa[40] describes a very radical procedure which includes maxillectomy with removal of the ethmoid and orbital contents, portions of the masseter and temporal muscles, the contents of the zygomatic fossa, the upper part of the ascending mandibular ramus, and, if necessary, the pterygoid plate and pterygomaxillary fossa. The internal maxillary is ligated. Six out of nine advanced cases have survived, although the postoperative period is still too short for final evaluation.

Erich and Kragh[41] review the results at the Mayo Clinic in a ten-year period including 174 cases. These were cases of squamous cell carcinoma of the antrum and upper jaw with 39.4 per cent five-year survival. In the early years surgical diathermy was employed. More recently they have been performing total maxillectomies followed by irradiation. Cervical metastases were found in 8.6 per cent before operation. In 30 cases, metastases were present subsequent to surgery. Block neck dissection was followed by irradiation, the latter was found to be of not too great value.

Fitz-Hugh and Gorman[42] object to preoperative irradiation, because primary regression can be misleading and thus influence subsequent surgery. Their procedure is wide block resection with exenteration of the orbit if necessary. Cauterization is not employed routinely but at times may be useful. Raw areas are immediately covered with skin graft.

Montana and Hedges[43] had four cases in which the orbit was involved and in which surgery followed by irradiation was not successful. They claim that these patients often see the opthalmologist first, at which time the growth has already reached extensive proportions. It should be pointed out, however, that otolaryngologists who also bemoan the lack of early symptoms are not quite so pessimistic.

Pietrantoni and Fregni[44] find planagraphs useful in determining the extent of the lesion and often deciding its operability. If the orbital contents must be removed, the authors refrain from covering the defect with a graft, as it may only conceal a recurrence and delay its detection.

Hessberg[45] claims 31 to 35 per cent five-year cures employing radical resection, surgical diathermy and removal of orbital contents if necessary. This is followed by radioactive Cobalt therapy up to 4000 r. Later, after healing has taken place, he gives an additional 3000 to 5000 r. by conventional deep X-ray therapy. Lymph nodes are irradiated early but usually have to be followed by neck dissections.

Ishrat-Husain[46] follows a procedure which he ascribes to F. Boyes Korkis but which seems to be quite similar to those mentioned by the above authors. He uses the diathermy knife through the soft tissues, and after the exenteration, applies Cobalt therapy.

Barocci and Massacesi[47] refer to Ohngren's arbitrary division of the maxilla by an imaginary line extending downward and backward from the internal angle of the orbit to the angle of the mandible forming two segments, the posterior one housing malignant tumors which are less favorable for a cure than the anterior segment. They use surgical diathermy in the hope of sealing off the lymphatics.

A comprehensive review of a series of 75 cases of malignancy of the sinuses treated in East Africa by Clifford[48] reveals some interesting facts. Apparently malignancy of the nose and sinuses is more common in hospital patients in East Africa than in Europe or America, and sarcoma in children is also more frequent. Some of the cases illustrated exhibit growths of enormous proportions. Most of the cases were extensive so that radical *bloc* excision was the only feasible approach. Considering the advanced state of many of these cases it is remarkable that the author was able to achieve as good results as he did. Fourteen out of 47 patients who underwent surgery are alive and well, although the period is not given.

Biarati and Pace[49] claim superior results in the treatment of malignant tumors of the maxilla through pseudopendulum stratigraphic delivery of the rays according to a method they ascribe to G. G. Palmieri *et al.* (Strati-Terapia—Ed. Cappelli, 1955). This appears to be similar to our rotation delivery of Cobalt 60. This method of concentration by movement in a unilateral direction resulted in 53.8 per cent three-year survivals.

Barth, Blumlein, Brichzy and Garal[50] recommend contact Roentgen therapy for inoperable malignancy of the antrum or in cases of recurrence by way of a pointed anode tube introduced into the cavity through the surgical opening. The latter may be in the palate, the face or the orbit after enucleation. It is claimed that smaller doses can be thus delivered to the tumor bed with no trauma to the healthy tissues. The apparatus they employed is made by the Siemans-Reiniger Company. Cures were obtained in 18 per cent of the 34 carcinoma cases, 40 per cent of the ten sarcomas and no results in three cases of other types.

Chaudhry, Gorlin and Mosser[51] review a series of 61 cases of carcinoma of the antrum, discussing incidence, symptomatology, pathology and diagnosis. Most of their cases were well advanced when first seen. Five-year cures were obtained in 10 per cent of the cases. They stress the importance of careful dental analysis since 24 per cent of their cases were

so related. It is also interesting to note that in 88 per cent of the cases, X-ray evidence of bony involvement was already present.

Invernizzi[52] reports a case of anaplastic epidermoid carcinoma of the maxilla involving the antrum in a child of nine. It started as a non-inflammatory swelling of the cheek and the X-ray pictures revealed destruction of the posterior wall of the sinus with invasion of the pterygoid. Two biopsies (nasal and nasopharyngeal) were reported as non-specific granuloma. A third biopsy via the sublabial approach yielded positive proof of malignancy. The child was treated with irradiated Cobalt receiving a total dose of 5500 r. The primary result was good.

Oberheuser, Schubert, Schuchardt and Spiessl[53] report good results in the treatment of malignant tumors of the oral cavity and the maxilla from the use of electron therapy via a 15 MeV-Betatron. Diagrams show the percentages of depth dose in various locations through fields varying from 6 x 10 cm. to an average 7 cm. This procedure envisions the inclusion of the lymphatics with the primary lesions.

Kobes[54] describes a prosthesis he constructed to hold a Co^{60} applicator in the treatment of a recurrent carcinoma of the mouth. The patient was a woman age 63 in whom a carcinoma of the upper lip, which resulted in the loss of substance, developed a recurrence involving the alveolus nasal floor and part of the mandible. Attached to the prosthesis was a telescopic extension which facilitated quick placement of the applicator in the mouth.

Mercier and Jezegabel[55] report two cases of carcinoma of the ethmoid in which exophthalmos was the first symptom. They urge careful study of planographs in such cases, since the conventional pictures may fail to show the lesion.

Mitchell[56] reports a case of carcinoma of the frontal sinus, in a man of 74, which at first was mistaken for a mucocele. Exposure and excision of the mass, followed by radiation therapy, proved ineffective since recurrences and extension to adjacent areas followed in a short time. Post mortem

revealed widespread carcinoma involving the orbit, base of the skull and brain. The author feels that perhaps a more radical exenteration at the first interference might have forestalled the recidivation.

Garrett[57] reports six cases of malignant tumors of the sinuses due to metastases from other locations. The primary lesions were in the testes, breast and lungs. This constituted 8 per cent of all the malignancies of the sinuses at the Liverpool Clinic in a two-year period. The author shows some slides representing the identical histology in the primary and metastatic areas.

Ravid and Esteres[58] report two rare cases of melanoma of the nose: one malignant, in a woman of 57; the other, benign, in an infant of eight months. The former manifested itself by nasal obstruction and bleeding and on examination revealed a dark polypoid mass originating in the inferior meatus. The biopsy specimen was diagnosed as malignant melanoma. The tumor was excised widely with removal of part of the maxilla and antrum. Within a month the patient was found to have X-ray evidence of lesions in the calvarium, the ribs, vertebrae and both femurs. The patient survived only six weeks after admission, and necropsy revealed metastatic lesions widely distributed throughout the entire body.

The author shows a number of microphotographs of histologic sections which demonstrate the typical findings.

The juvenile melanoma appeared in the left nasal cavity of the eight-month-old infant and was readily removed. It was found to be attached by a narrow pedicle to the posterior portion of the nasal vestibule. Histologically it was shown to be a typical benign melanoma. The sections shown demonstrate the histologic differences between it and the other malignant type.

Embryonal rhabdomyosarcoma of the nose is rare. The case reported by Allen[59] was in a woman of 46 whose complaint was a swelling on the right side of the nose and epiphora. Examination revealed a reddish grey mass in the vestibule, and X-rays showed cloudy maxillary ethmoid and

frontal sinuses. Biopsy was diagnosed as rhabdomyosarcoma. The tumor was removed via a Weber-Ferguson approach and was found to be attached to the lateral wall of the nose. It extended into the antrum and involved the medial wall and floor of the orbit. The orbital contents, floor of the orbit and antrum were exenterated. Since the ethmoids were also involved they were cleaned out clear up to the dura. Some postoperative leakage of cerebrospinal fluid was observed for a short period. All raw surfaces were covered with Thiersch grafts. There was no evidence of recurrence when examined 18 months later.

Ross[60] had a case of ameloblastoma arising from the alveolar process in a 13-year-old boy. The unusual feature of the tumor was the "transformation of its cells into a kind of 'ghost epithelium' which elicited a foreign body reaction."

These cells histochemically represented aberrantly keratinized and calcified cells. Some very fine microphotographs illustrate the various histologic aspects of the tumor.

A case of olfactory neuroblastoma of the antrum in a man of 24 is reported by Washberg *et al.*[61] The symptoms were not characteristic, chiefly pain and swelling of the eye. X-ray pictures showed a mottled, calcific shadow filling the antrum. At the same time there was an oroantral fistula following prior removal of two molars. The mass was removed via a Caldwell Luc and the fistula repaired. A photomicrograph of the nasal mucosa showed closely packed cells in a neuroid stroma.

These tumors are not metastatic but are believed to be invasive in character.

Church and Uhler[62] report a case of neuroblastoma of olfactory origin which involved the maxillary region and extended into the orbit and nasal cavity. Two wide excisions of the superior maxilla within six months of each other failed to halt the process which ended fatally. The authors state that the tumor is rare, and they explain the pathogenesis as being due to an embryological fault whereby cells of the

olfactory system are displaced or left behind during the development of the maxilla.

Of the five cases of plasmocytoma reported by McCall[63] three involved the sinuses. Although all were radically removed and received extensive radiotherapy, only one survived.

Microscopically, these tumors are identical with multiple myeloma, being of lymphatic origin. Although radio sensitive they tend to metastasize unless excised at an early stage of the process.

The microscopic features of the tumor reveal plasma cells of various sizes with abundant cytoplasm with eccentric nuclei having a spoke-like configuration of the chromatin material.

Calle and Chavanne[64] discuss the radiologic aspects of certain unusual tumors of the maxilla showing, by means of X-ray pictures and laminagrams, the extent and limitations of these tumors. The cases illustrated represent typical cylindromas, lymphoepitheliomas and adamantinoma. Cylindromas appear as a dense opacity "balloon like" with slow invasion of the bony walls. They develop slowly and are sensitive to irradiation. Lymphosarcomas show a homogeneous density with late involvement of the bone; they also are radio sensitive. Adamantinomas present a cystic or multilocular appearance in the X-rays similar to that seen in myeloplaxes and plasmocytomas. They grow slowly and tend to recur despite irradiation. Radical surgery offers the best chance for a cure.

Brown and Woolner[65] report six cases of Wegner's granulomatosis with autopsy findings in four. One patient, a girl of 14, survived. The case was evidently a mild one. The authors agree with other observers that this syndrome and lethal midline granuloma are one and the same, even though in some instances the involvement of internal organs was not observed. Analysis of most cases shows that the process begins in the upper respiratory tract and later involves the internal organs such as the lungs, kidneys, liver and spleen.

The characteristic autopsy findings are those of a generalized periarteritis nodosa. Failure to demonstrate it in the biopsies from the nose and throat may be due to incomplete search throughout the entire specimen.

In none of the cases cited was there any evidence of reticulum cell sarcoma which some observers seem to think is the real cause of the process.

Chilese[66] reports a case of malignant granuloma in a 22-year-old patient. It started with a furuncle in the nasal vestibule. This was followed by redness and swelling of the nasal labial fold and cheek, temperature and necrosis. The process developed rapidly into a massive destruction of the entire maxilla extending into the orbit and oral cavity. Every diagnostic facility was employed in an attempt to arrive at a diagnosis. Syphilis, Leishmaniasis, malignant tumor, mycosis and bacterial infections were eliminated. Therapeutics employed included various antibiotics, tartar emetic, radiation therapy, arsenicals, iodides and antimycotic agents all to no avail. No mention was made of the use of steroids although it was suggested.

Tamura and Sato[67] report two cases of gangrenous granuloma of the nose which recovered. In one case there was a metastasis to the submaxillary gland; in the other case, the symptoms were aggravated after removal of the initial lesion. In both of these cases it was found that although the superficial layers of tissue were histologically undetermined granuloma, the deeper layers revealed typical findings of a lymphatic reticulosarcoma which confirms what other authors have stated, namely, that some cases that appear to be malignant granuloma prove to be otherwise when the tissues are exhaustively examined.

Link[68] is not willing to concede that granulomatosis is basically a periarteritis nodosa as claimed by some. Both of his cases were primarily lesions of the nose and sinuses with other lesions in the musculature as well as internal organs, conforming to the Wegner's syndrome; yet both patients underwent a radical antroethmoid exenteration and recovered

under steroid therapy. Although the histologic findings conformed to those usually ascribed to Wegner's syndrome, the resolution of the process following Cortisone therapy leads the author to conclude that his cases were probably abortive Wegner's.

These cases belong to the group of inflammatory allergic ailments, clinically polypoid; histologically, granulomatous. Because the upper respiratory area is the first area of contact with most allergens, it is here that the antigen-antibody reaction takes place. Beneath the simple polypoid aspect lies a deeper special microscopic morphology—this points to the need for more extensive examination of these tissues.

Czigany[69] reports a case of adamantinoma involving the maxillary sinus and nasoantral wall. It protruded through the nares and could be seen postnasally. It was removed intranasally along with the inferior turbinate and a portion of the middle turbinate. It was not followed by irradiation therapy which as a rule has little effect on these tumors.

NONMALIGNANT TUMORS.

Case reports of osteoma of the sinuses have been numerous. Among them are several with serious intracranial complications.

Schneck's[70] case was associated with marked orbital symptoms that came on suddenly with a spontaneous vertical nystagmus. The former were explained as being the result of a periostitis with involvement of the sphenoid fissure, but the nystagmus was totally inexplicable since there were no signs of meningeal involvement. The author speculates on the possibility of an extension of the periostitis to the base of the skull via branches of the Vth nerve. (The possibility of contracoup pressure on the cerebellar and basal nuclei causing irregular nystagmus was raised some years ago by DeKleyn and Versteegh: Zeit. f. H. N. O., Vol. 21, p. 295—S. S.)

In the case reported by Logue and Sights, Jr.,[71] in which a dural defect was not adequately closed at the first interven-

tion, the patient suffered a second attack of meningitis following the postoperative rhinorrhoea. Secondary operation with closure of the dura effected a cure.

Boenninghaus' case[72] of an osteoma of the ethmoid was associated with a pneumatocele in the fronto-parietal region with pressure on the left hemisphere causing paresis of the hand and foot. The dural defect was closed with a rotating periosteal flap from the frontal bone.

Hariga[73] reports an interesting case in which there was a history of trauma about a year ago. At this time headaches and a discharge of cerebrospinal fluid led to the discovery of an opaque mass above the orbit and a dilatation of the posterior horn of the contralateral lateral ventricle. When meningitis supervened a frontal craniotomy was performed, revealing the osteoma which was covered by a huge polyp and also a communication between the frontal sinus and the lateral ventricle. Apparently the trauma previously sustained caused a fracture of the posterior wall of the frontal sinus.

In the case reported by Montrieul *et al.*[74] a large fronto-ethmoid osteoma was exposed by a coronal incision and found to have eroded the posterior wall and dura. This defect was closed by rotating a large epicranial flap.

Eckel and Palm[75] were interested in the incidence of osteoma which is difficult to determine, because so many of these growths are silent. They found that in a study of 15,947 consecutive X-rays of the skull there were only 66 cases. They estimate that on the population at large the incidence is about .4 per cent.

Osteomas of the maxillary sinus are infrequent. Jordan[76] reports one, in a 16-year-old girl, which was successfully removed via a partial maxillectomy. Lentine and Saeed[77] also saw one in a 16-year-old girl which was not operated. They also had three cases involving the frontal sinuses which are well documented by fine X-ray pictures and histologic sections, showing a beautiful illustration of the spongy type. Ganz's case was in a man of 59. The growth arose from the

floor of the antrum. In this case also there was history of trauma many years ago.

This brings up the question of the etiology insofar as trauma is concerned. Eckel[78] cites Dietrich as having assembled histories of 62 cases in which prior trauma was noted. Speculating on the medico-legal aspect of these cases the author finds that the criteria set forth by Lubarsch, which would be valid in establishing cause and effect, were lacking in all of these cases; nevertheless, there have been cases in which the growth of an osteoma was accelerated by trauma.

There have been two reports on the osteoplastic approach for the removal of frontal osteoma. The one by Newell *et al.*[79] was done by the technique suggested by Goodale. Two cases reported by Montgomery[80] were also handled in the same manner. The cavity was filled with abdominal fasci-fat implant. The cosmetic result was excellent. The article is well illustrated, showing the technique as well as the X-ray pictures.

Kecht[81] also removed one from a 16-year-old girl through a coronal exposure and an osteoplastic flap. Since both frontals were involved, he removed the posterior walls of the sinuses allowing the dura and frontal lobes to fill the space thus obliterating the cavities.

Snyder's[82] case of an osteoma of the ethmoid was in a boy of 17, with a history of prior trauma which seemed to accelerate the growth of the tumor which at the time of the accident was very small.

Tanzer[83] claims that osteoid osteoma is rare about the skull. He points out the characteristic findings in the X-ray pictures that differentiate it from an osteoma.

Sorensen[84] had five cases of fibro-osteoma of the maxilla and antrum. Because of the erratic manner of growth it is often difficult to exenterate these tumors completely. He describes a method of fixing free grafts in the cavity after resection.

Ariagno and Oppenheimer[85] saw a case of leiomyoma in-

volving the maxillary sinus in a woman of 59, which presented a swelling through the lip and was thought to be a mucocele. When exposed it was found to be solid and very vascular and had eroded all the walls of the sinus, obliterating the ethmoid cells and extending into the pterygo maxillary fossa. It weighed 90 gms. and measured 7.5 cm. at its greatest diameter. Sections disclosed whorls of palisading cells composed of pale eosinophiles with fine granular cytoplasm and large basophilic nuclei. The authors claim that this is the first of its kind in this area to be reported.

A case of chondroma of the maxilla in a man of 48 reported by Cimini[86] was present for 36 years before it began to take on renewed activity following trauma to the face, and rapidly developed into a chondro-sarcoma. Since the maxilla is not cartilaginous, either in embryo or the adult, it is assumed that the growth originated either from a development rest or from a metaplasia.

Two cases of mucocele of the frontal sinus are reported by Cruz[87] in which both the orbit and cranial cavity were invaded. X-rays showed the extent of the growths, and angiography proved helpful in one case by outlining it. They were both successfully removed via a frontal osteotomy.

McHenry *et al.*[88] report a case of mucocele of the sphenoid sinus which suggested a possible malignancy, because the X-rays showed destruction of portions of the bony walls with encroachment on the pituitary. It was exposed via an external ethmoidectomy. The cystic cavity contained about 60 ml. of fluid. The dura was exposed over an area of 2.5 cm.

Lederer[89] reviews the history of nasal polypi all the way back to the ancients and discusses recent investigations which have as yet failed to disclose the true nature of the phenomenon.

A case of fibrous dysplasia with monster-like deformity is reported by Markowicz and Shannon[90] in a 25-year-old male. The growth was so extensive as to displace the bulb, the nose and the entire half of the face. An attempt to remove it resulted fatally from uncontrollable hemorrhage.

According to Tsikoudas[91] simple fibroma of the antrum is uncommon; juvenile fibroma and benign giant cell tumors are frequently encountered. The case he reports was in a five-year-old girl in whom the mass caused an upward displacement of the bulb and nasal obstruction. It was removed via a sublabial approach. It apparently originated from a spine near an ectopic premolar. Histologic examination revealed abnormal growth of connective tissue with rare elliptic, spindle and stellate-shaped cells.

Pirodda and Orru[92] present a lengthy and well illustrated article on "Bleeding polyps of the septum" based on their studies of 35 cases, three of which involved the turbinates, and a discussion of theories advanced by other observers. Histologic study reveals a characteristic pattern of a venous network formed by dilated and congested vessels with thickened or polypoid protuberances and with proliferation of the endothelium. It is their belief that these growths are due to functional alterations in the local circulation arising from abnormalities in the regulatory system, especially the arterio venous anastamoses. Inflammatory reactions may or may not be present but, in their opinion, are not etiologically significant. They point to a similarity with analogous growths such as telangiectatic granuloma, hyperplastic angioma and pseudobotriomycoma which are found in localities such as the finger tips, nail bed, lip, gums, etc., which are rich in regulatory formations of the local circulation.

Terracol and Guerrier[93] list the various types of benign tumors found in the sinuses, dividing them into three main groups: those of monodermic or didermic structure; those derived from heterotopic tissues, vestigial or acquired, and the dysembryonic tumors. Chondroma and osteoma are examples of monodermic structures. Didermic tumors contain two types of tissue, namely, epithelial and glandular, as typified by papilloma adenomas.

Heterotopic tumors would include chordomas.

Dysembryonic tumors are represented by rhabdomyomas.

Other growths of different origin are neurogenic tumors, myeloplaxes and cholesteatoma.

The authors describe these different types of tumor and briefly indicate the therapy.

Weaver[94] discusses briefly neoplasms of the frontal sinus mentioning several malignancies successfully treated and reporting a very large mucocele in a woman of 74.

Packard and Baxter[95] report a very unusual case of an aneurism in the superior maxilla of a 13-year-old girl. Nose bleed was followed by profuse hemorrhage from a fistula above the first molar which persisted and necessitated ligation of both external carotids. The swelling of the face continued unabated, and it was finally decided to resect the maxilla which was successfully accomplished, though attended by severe hemorrhage. The specimen showed a huge aneurism which had occupied the greater part of the maxilla and antrum. The patient was rehabilitated through the employment of an adequate dental prosthesis.

Mark and Levin[96] had a case of a dentigerous cyst associated with a supernumerary molar in which the only problem was the question of direct involvement of the sinus. The X-ray pictures, especially the Waters view, were of great help.

According to Piquet and Benoit[97] who describe three cases of hemangioma of the ethmoid, these growths can be divided into two groups: one group includes cases that are primarily inflammatory granulomas with hemangiomatous features such as extensive dilated capillary formations with endothelial proliferation in an edematous stroma; the other group comprises cases of the polypoid type. The association of the angioma with the polyp can be explained in two ways: either primary angioma causes a secondary edema with polyp formation, or by blocking the sinus ostiums setting up a sinusitis, which in turn may produce polyp.

Ganz,[98] reviewing available statistics of other authors, finds that the antrum was involved in 5.5 per cent of all cases of osteoma of the sinuses. He reports a case in a man of 59

where the growth arose from the floor of the antrum and showed fatty marrow within its spongy substance. There was a history of severe trauma many years ago which may have been the etiologic factor.

SURGERY.

Recently increased interest has been manifested in osteoplastic procedures in frontal sinus conditions and obliteration by fat, gelfoam or bone chips. The first six abstracts that follow deal with this subject.

Lovo[99] finds abdominal fat superior to iliac bone for filling the cavity because it is easily obtained and can be moulded better. He suggests taking the fat from the lower abdomen and allowing for shrinkage by packing as much of it into the cavity as possible.

Mozolewski[100] hinges his bony flap above rather than below. He enters the sinus through a brow incision and the floor of the sinus removing its contents and then reflecting the bone flap upward. The cavity is filled with fat or gelfoam.

Rongetti[101] suggests a similar approach which he employed for the removal of an osteoma. This method is especially adaptable for cases in the duct, and ethmoids are not involved.

Schwartzmann[102] also used a bone flap in a case where only one frontal was affected, but the opposite sinus was uninvolved. He constructed a partition with bone from a bone bank and filled the sinus with a material, the nature of which he fails to mention.

Himmalstein[103] reports two cases of chronic frontal sinusitis in which he obliterated the sinus with gelfoam. The results were satisfactory, except for a slight loss of contour.

Overbosch and Rap[104] used a bone flap through a coronal incision and filled the cavity with small pieces of cancellous iliac bone.

Hirsch,[105] whose pioneer work in the development of the transseptal sphenoid approach to the hypophysis is well

known, reports an unusual case, the first of its kind to be successfully treated in this manner. The patient was a girl of three and one-half (a twin) whose vision had rapidly deteriorated to light perception due to a tumor of the pituitary stalk cranio-pharyngeal. Since the growth was below the sella it was not amenable to a transfrontal intracranial approach; however, to reach the growth via the transseptal route was extremely risky, because it was necessary to go through the thick mass of the sphenoid body without the customary landmarks. After three attempts the sphenoid body was finally penetrated with a long dental burr attached to a specially constructed handle which permitted good visualization, the mass was reached and its liquid contents aspirated. Although the vision rapidly improved, the progress came to a standstill, and it was determined that the fistulous tract had closed. The patient was reoperated and better visualization was afforded through sublabial exposure of the septum. This time a tantalum tube 2.5 cm. long and 4.5 mm. thick was introduced into the tract which again had to be widened. This had the desired effect in promoting drainage. The cystic cavity eventually collapsed, and the area was filled in with cicatricial tissue. The patient was followed for ten years during which time the vision returned to normal in one eye, the other having long since undergone optic atrophy. The metal tube was still in place. The child's general development proceeded normally.

Rasmussen[106] describes his modification of Hirsch's operation which was successfully carried out in 13 cases. The columella with about 1 cm. of septal cartilage is detached at its base and reflected to one side. The incisions in the mucosa are staggered so as not to superimpose. The septum is then resected back to the sphenoid and the mucosa covering the anterior wall dissected off to one side. After the sphenoids are opened, a probe is inserted, and the location of the pituitary fossa is identified by an X-ray picture. Then the posterior sphenoid wall is removed, exposing the dura, which is incised in an upside down incision and the gland then removed piecemeal if not *in toto*. The cavity is then filled with gelfoam, the septal mucosas approximated and held together

with finger-cot plugs after which the columella is sutured back. The author shows a self-retaining speculum which he found useful for the exposure.

Three patients developed a liquorrhea, but none, meningitis. No other complications were noted except some headache for a few days.

Williams[107] presents an analysis of the results obtained over a period of 17 years in 59 external ethmoid operations by the Patterson technique, only those cases that were examined after a lapse of three years were considered. He found relief of obstruction in 93 per cent of the cases; relief of discharge in 85 per cent; headache in 90 per cent, polypi recurred in 9 per cent. The general health was improved in 57 per cent of the cases. The author shows the anatomy of the area and describes the technique. Its advantage over the transantral and intranasal routes is greater accessibility to the most anterior group of cells.

Hamberger *et al.*[108] describe three cases of cranio-pharyngioma which were successfully removed via a transmaxillary sphenoid approach. A prior transfrontal exposure demonstrated the growths to be suprasellar and extending backward almost to the third ventricle. It would have been impossible to remove the tumors through this exposure because of the involvement of the chiasm. The practicability of the transmaxillary they used proved itself in these cases. Even the upward extension could be drawn downward without damaging the chiasm, and the vision subsequently returned to normal.

Brunetti and Rossi[109] describe a technique for reaching the hypophysis via a transfronto-ethmoid exenteration into the sphenoid. The details are somewhat complicated, but the authors assert that the passage afforded allows adequate room for dealing with hypophysis.

Ogura, Watson and Jurema[110] attempt to reconstruct the nasofrontal duct by means of two mucoperiosteal flaps derived from the septum and lateral nasal wall. The ascending process of the maxilla is removed along with the lacrimal bone and

the bone lying anterior to the cribriform plate which represents the root of the perpendicular plate and nasal septum. It is also necessary to remove a wedge of bone lying between the medial portions of the frontal sinuses and bridge of the nose. The operation was performed bilaterally in 17 cases.

Terracol *et al.*[111] discuss the complexity of the fronto-ethmoid complex and recommend the transantral approach popularized by Piantratoni de Lima and Tato, although they call attention to the work of Moure and other French authors which clarified the anatomic details and paved the way for the development of the transantral operation.

Bordley and Cherry[112] since September 1940 have performed 40 rhinotomy procedures for a variety of conditions listed under three heads: infection, cysts and tumors, and malignant tumors. The infection cases were of long standing with history of unsuccessful surgery resulting in loss of landmarks, scarring and degenerative changes. Twelve cases of cysts and unusual tumors such as encephalocele, chromophobe adenoma of the pituitary, etc., are listed. There were 17 cases of malignant tumor of various types.

The indications for this procedure are cases where the conventional technique fails to afford adequate exposure and visualization of the area. The technique is described with accompanying drawings, and the cosmetic results which were admirable are shown in two cases.

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(Continued in November Issue.)

SIXTH INTERNATIONAL CONGRESS OF AUDIOLOGY.

The Sixth International Congress of Audiology will be held in Leyden, The Netherlands, September 5-8, 1962.

President: Prof. Dr. H. A. E. van Dishoeck;

Secretary: Dr. A. Spoor.

The program will include three round-table talks on "Frequency analysis of the normal and pathological ear." Moderator: Prof. Dr. G. von Békésy. "Central deafness in children." Moderator: Prof. Dr. J. M. Tato. "Psychogenic deafness and simulation." Moderator: Prof. Dr. H. A. E. van Dishoeck, and associated and independent papers.

Official languages of the Congress are: English, French, German and Spanish. Working languages will be: English and French.

For further information address the secretariat, Ear-Nose-Throat Department, Academisch Ziekenhuis, Leyden (The Netherlands).

THE GEORGE E. HODGE MEMORIAL AWARD.

At the Annual Meeting held in Montreal, June 15, 1961, the Canadian Otolaryngological Society established an Annual Award for the best paper presented by a member of the Society or by a resident of otolaryngology in training.

The purpose of the award is to stimulate the writing of papers by young otolaryngologists. There is no limitation as to the subject and includes all phases of otolaryngology (clinical work, clinical or experimental research).

The award, called the George E. Hodge Memorial Award, is named to commemorate the first President of the Society. The award consists of a suitably engraved plaque and a cash prize. The successful author will read his paper at the Annual Scientific Programme. The presentation of the monetary rewards, engraved plaque and attestations will take place at the Annual Meeting.

The manuscript must be typed, double spaced on letter size (8½" by 11") paper. The author must not sign his name on the manuscript but must use a pseudonym. His surname and Christian name are to be written in a separate envelope, sealed and sent to the Secretary of the Canadian Otolaryngological Society, 174 St. George St., Toronto 5, Ontario, the pseudonym appearing on the outside of the envelope. The closing date for the submission of the manuscript, in triplicate, to the Secretary, is the 31st day of January.

An award committee of three, appointed by the president and his council, will judge the manuscripts and their decision will be final. No award will be given if, in their opinion, the manuscripts are not worthy of an award. Two awards may be given in any one year. The decision of the Committee will be based upon the scientific and clinical value to otolaryngology, and upon the originality of material.

DIRECTORY OF OTOLARYNGOLOGIC SOCIETIES.

(Secretaries of the various societies are requested to keep this information up to date).

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President: Dr. Lawrence R. Boies, Milwaukee, Wisc.
Executive Secretary: Dr. William L. Benedict, Mayo Clinic, Rochester, Minn.
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AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION.

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Meeting:

AMERICAN BOARD OF OTOLARYNGOLOGY.

President: Dr. Gordon D. Hoople, 1100 E. Genesee Dr., Syracuse 10, N. Y.
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Meeting: Sheraton-Dallas Hotel, Dallas, Tex., May 1-2, 1962 (afternoons only).

AMERICAN LARYNGOLOGICAL ASSOCIATION.

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Editor, Historian, and Librarian: Dr. Francis W. Davison, Danville, Pa.
Meeting: Sheraton-Dallas Hotel, Dallas, Tex., May 4-5, 1962.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, INC.

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Annual Meeting: Sheraton-Dallas Hotel, Dallas, Tex., May 1-2-3, 1962 (mornings only).

AMERICAN MEDICAL ASSOCIATION, SECTION ON LARYNGOLOGY, OTOLOGY AND RHINOLOGY.

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Secretary of Ophthalmology Section: Dr. Philip D. Shanedling.
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Secretary of Otolaryngology Section: Dr. Francis O'N. Morris.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd., Los Angeles, Calif.
Time: 6:30 P.M. last Monday of each month from September to June, inclusive—Otolaryngology Section. 6:30, first Thursday of each month from September to June, inclusive—Ophthalmology Section.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY.

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Secretary: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.
Meeting: Edgewater Gulf Hotel, Edgewater Park, Miss., April 13-14, 1962.

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(Nederlandsche Keel-Neus-Oorheelkundige Vereeniging.)

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Meeting: Fourth Tuesday of each month from September through May, Aero Club, Portland, Ore.

OTOSCLEROSIS STUDY GROUP.

President: Dr. Arthur L. Juers, 1018 Brown Bldg., Louisville, Ky.
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Meeting: Las Vegas, Nev., November 2, 1962.

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President: Dr. Plino de Mattos Barretto, Sao Paulo, Brazil.
Acting Executive Secretary: Dr. Charles M. Norris, 3401 No. Broad St., Philadelphia 40, Pa., U. S. A.
Meeting: Eighth Pan American Congress of Oto-Rhino-Laryngology and Broncho-Esophagology, Puerto Azul Club, Valencia, Venezuela, S. A., February 25th to March 1st, 1962.

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